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Original Article

A Step towards Patient Safety by Comparing a Trigger Tool with Pre-Existing Tools in the Pharmacovigilance

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ABSTRACT

Aim: To develop a trigger tool for the assessment of Adverse Drug Reaction in hospitalized patients and to compare them with pre-existing tools and validating the new ADR assessment tool. **Materials and Methods:** A prospective observational study was conducted in tertiary care teaching hospital for a period of six months. 43 patients were selected for the study. The adverse drug reactions were assessed and compared with pre-existing ADR assessment scales with validated SVCP-ADR assessment scale for screening the suspected adverse drug reaction. **Results:** Total 43 ADRs were reported during the study period, out of which 24 ADR were found in males (56%) and 19 in females (44%). When comparing the SVCP-ADR assessment scale to the five other ADR assessment scales, it showed a higher frequency of positive outcomes (81.39%) compared to the three of those scales. **Conclusion:** In this study, a tool was created and validated with a content validity index of 0.9 to facilitate the evaluation of Adverse Drug Reactions (ADRs). Furthermore, the results obtained from the five scales such as WHO causality assessment scale, Naranjo Probability scale, Hartwig and Siegel severity scale, Schumock and Thornton scale, Liverpool Avoidability scale were divided into positive and negative outcomes and these outcomes were compared with the SVCP-ADR assessment tool. The study revealed a notable increase in positive outcomes in our tool when compared with the other three scales such as Hartwig and Siegel severity scale, Schumock and Thornton scale, Liverpool Avoidability scale.

Keywords: Pharmacovigilance, Adverse drug reaction, Trigger tool, Validation.

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INTRODUCTION

Pharmacovigilance is defined by the World Health Organization as 'the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other drug-related problem.[1,2] Pharmacovigilance's main goal is to guarantee the safe and efficient use of pharmaceuticals by detecting and assessing any possible hazards or problems that might occur while they are being used.[3] According to WHO, an ADR can be defined as any response of a drug which is noxious and unintended, that occurs at doses used in humans for the prophylaxis, diagnosis or therapy of disease; or for the modification of physiologic function purposely excludes therapeutic failures, overdoes, drug abuse, non-compliance and medication errors.[4]

A method for determining if a medication may have contributed to an adverse drug reaction is called causality assessment. It determines the extent of the relationship between a medication and a potential ADR. It is done to identify serious adverse drug reactions, generate alerts and evaluate the efficacy and safety of prescription drugs.[5]

A trigger tool in pharmacovigilance is a technique or system that finds possible adverse drug reactions or safety alerts in significant data sets, including databases of spontaneous reports or electronic health records. It involves utilising predetermined criteria or certain triggers to identify possible ADRs and mark them for more research.[6-8] In pharmacovigilance, a trigger tool is a proactive method to find possible adverse drug reactions by methodically looking for predetermined triggers or criteria in large databases. These triggers could be particular occurrences, trends, or arrangements of data points that cast doubt on the possibility of a negative medication reaction. Triggers can include things like abnormal test results, certain diagnoses, medication adjustments, or clinical occurrences linked to known adverse drug reactions.[9-11]

The study is aimed to compare and evaluate the pre-existing ADR assessment scales with SVCP-ADR assessment tool for screening the suspected adverse drug reaction cases. To develop and validate a tool which is reliable and sensible for measuring ADRs.

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Various scales are employed for assessing adverse drug reactions, yet most of these scales come with their own advantages and drawbacks. The primary aim behind creating standardized methods for assessing adverse drug reactions is to establish dependable, consistent and validated data concerning the link between adverse reactions and suspected drugs

MATERIALS AND METHODS

This prospective observational study was done to develop a trigger tool for the assessment of Adverse Drug Reaction in hospitalized patients and to compare them with pre-existing tools and validating the new ADR assessment tool (Table 1). 43 patients were selected for the study. The adverse drug reactions were assessed and compared with pre-existing ADR assessment scales with validated SVCP-ADR assessment scale for screening the suspected adverse drug reaction (Tables 2 and 3).

Data collection occurred between March and August, 2023 by direct interview with patients and caretakers as well as self-designed data collection form were used to collect patient details like demographic details, diagnosis, past medical and medication history, laboratory reports and treatment given. The Adverse Drug Reactions were assessed using scales like WHO probability scale, Naranjo Algorithm, Hartwig and Siegel severity scale, Schumock and Thornton preventability scale, Liverpool Avoidability scale.

Inclusion criteria: Patients with age greater than 18 years old. Patients agreed to participate voluntarily with verbal consent. Patients who were admitted as inpatients in the study duration. Adverse event to poisoning/ drug abuse and dependence. Exclusion criteria: Children and Pregnant women. Patient not willing to participate in the study.

Microsoft Excel 2019 was used to analyze the data and results were assessed by descriptive statistics -Frequency Distribution.

Table 1: Method of study.

Steps	Method
Step-1	The target area for possible research was identified and finalized the project title.
Step-2	The aim and objective were framed and defined the criteria and standards.
Step-3	Literature survey.
	Sample size calculation.
Step-4	The data entry form was designed.
	Protocol was prepared.
	Approval from the IEC.
Step-5	Selected patient according to inclusion and exclusion criteria.
Step-6	Obtained informed consent.
	English informed consent form.
	Tamil informed consent form.
	Prospective collection of data.
	Data was collected from the patient by using self-designed data collection form.
Step-7	Development of assessment scale.
	Questions within the five scales reviewed. Consensus opinion to use flow chart.
	Framed a tool with eight elemental questionaries with YES, NO and UNSURE replies.
Criteria	Unevaluable. Possibly manageable. Definitely manageable. Not manageable.
Requirements	Temporal relationship.
	Plausibility.
	Detailed categorization of reaction.
	Laboratory findings.
	Presence of alternative causes.
Step –8	Expert consultation (3 Experts).
Step-9	Item refinement.
Step-10	Validation of SVCP-ADR assessment tool using validation form (Figure 1).
Step-11	Assess and compare 43 ADR cases using Five scales with new tool.
Step-12	Outcomes evaluated using the six scales were classified into positive and negative outcomes.

RESULTS

Gender wise distribution among the study population

The study population was categorized according to gender, which constituted a greater number of males. Out of the 43 patients included in the study 55.81% (24 patients) were male and 44.18% (19 patients) were female (Figure 2).

Age wise distribution among the study population

In the study, 62.79% subjects belonged to the middle adulthood group (58-77 years). 6.97%, 20.93% and 9.30% belonged to the age group of (18-37), (38-57) and (78-97) years respectively (Figure 3).

Department wise distribution among the study population

The total number of adverse drug reactions that has been occurred in various department were assessed and it was found that the majority of adverse drug reaction were occurred in cardiology department (51.16%) (Figure 4).

Systems presenting with adverse drug reaction among the population

Among the 14 systems, the most frequent system presenting with adverse drug reaction were skeletal system (23.25%) followed by metabolic system (16.27%) (Figure 5).

Frequency of types of adverse drug reaction among the population

Types of adverse drug reaction occurred among study population shows that majority of reaction belonged to Type A (69.76%) (Figure 6).

Frequency of most commonly occurred adverse drug reaction among study population

Among the adverse drug reaction occurred, the most frequently observed reactions were Amlodipine induced Pedal edema (18.6%) followed by Ticagrelor induced dyspnea (11.62%) (Figure 7).

Frequency of class of drugs associated with adverse drug reaction

Out of 7 classifications of drugs, the majority of the reactions were observed among the class of antihypertensives (27.9%) followed by antiplatelet agents (16.27%) (Figure 8).

Frequency of categorization of reaction among the study population

Among the study population, the highest number of reactions categorized and reported were adverse drug reactions (65.11%) followed by side effect (16.27%) (Figure 9).

Frequency of management of adverse drug reaction among the study population

Among the study population, 48.83% were not treated and continued with same medication and 13.9% of ADR were managed by withdrawing the offending drug (Figure 10).

Frequency of adverse drug reaction assessed by who causality assessment scale

The Causality assessment of the reaction was classified based on WHO causality assessment scale, in that majority of the reactions was observed under Probable (83.72%) category (Figure 11).

Frequency of adverse drug reaction assessed by naranjo algorithm scale

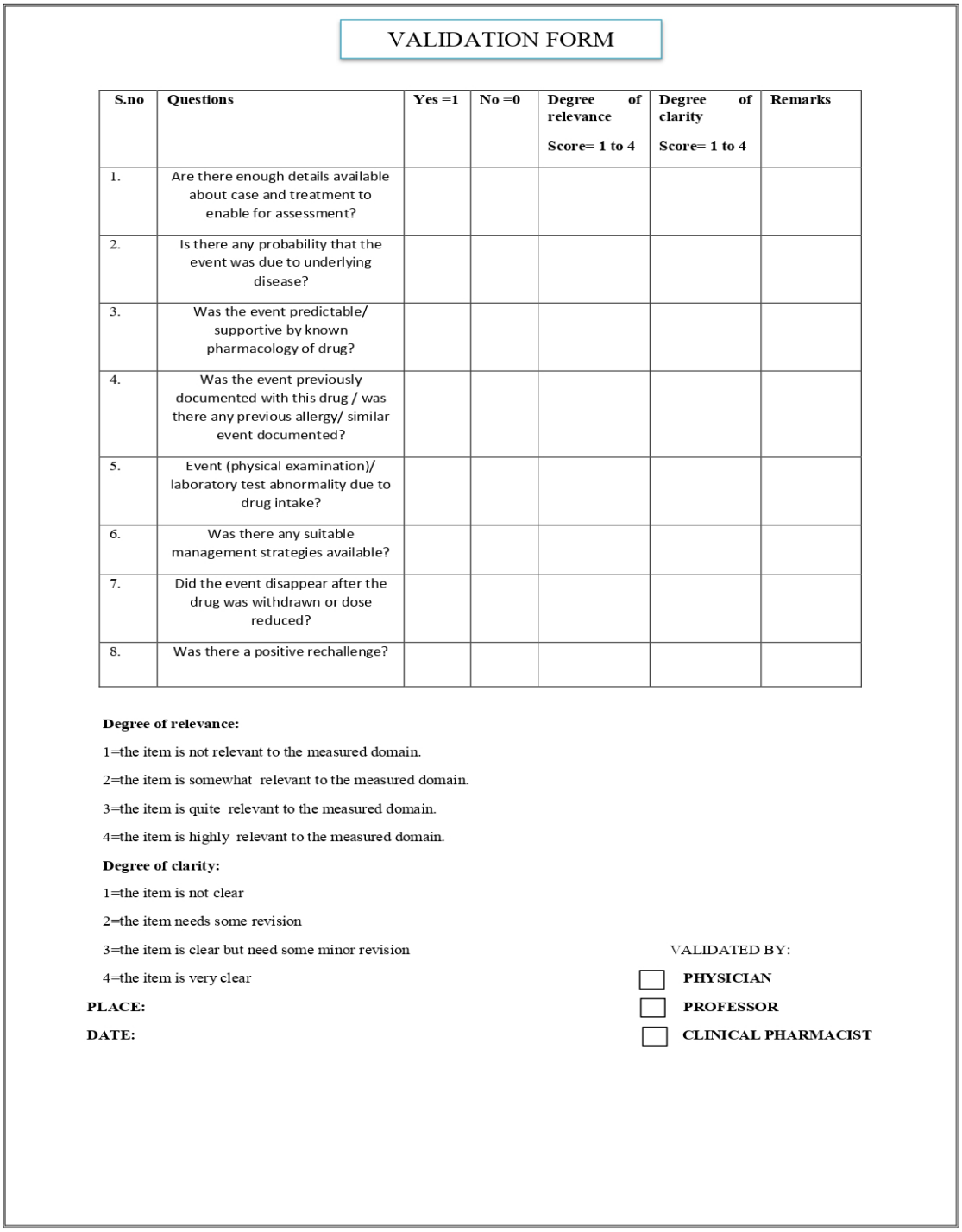
The Probability of the reaction was classified based on Naranjo Probability Algorithm scale, in that majority of the reactions were observed under Probable (86.04%) category (Figure 12).

Table 2: Procedure for validation.

Tool development	To develop an instrument to assess the adverse drug reactions.
Validation process (Phase 1)	Preparing a content validation form. Selecting a review panel of experts (Physician, Professor and Clinical Pharmacist).
Validation process (Phase 2)	Conducting content validation.[12] Reviewing domain and items.
Validation process (Phase 3)	Providing score on each item. Calculating Content Validity.

Table 3: Content Validity Index Calculation.

Domain knowledge	Relevance					
Item	Expert 1	Expert 2	Expert 3	Expert in agreement	I-CVI	UA
1	4	4	3	3	1	1
2	4	4	3	3	1	1
3	4	4	4	3	1	1
4	4	3	4	3	1	1
5	4	1	4	2	0.6	0
6	4	3	3	3	1	1
7	4	3	4	3	1	1
8	4	3	4	3	1	1
Proportion Relevance	1	0.875	1		S-CVI AVE=0.95	S-CVI UA AVE=0.9



VALIDATION FORM

S.no	Questions	Yes =1	No =0	Degree of relevance Score= 1 to 4	Degree of clarity Score= 1 to 4	Remarks
1.	Are there enough details available about case and treatment to enable for assessment?					
2.	Is there any probability that the event was due to underlying disease?					
3.	Was the event predictable/ supportive by known pharmacology of drug?					
4.	Was the event previously documented with this drug / was there any previous allergy/ similar event documented?					
5.	Event (physical examination)/ laboratory test abnormality due to drug intake?					
6.	Was there any suitable management strategies available?					
7.	Did the event disappear after the drug was withdrawn or dose reduced?					
8.	Was there a positive rechallenge?					

Degree of relevance:

1=the item is not relevant to the measured domain.

2=the item is somewhat relevant to the measured domain.

3=the item is quite relevant to the measured domain.

4=the item is highly relevant to the measured domain.

Degree of clarity:

1=the item is not clear

2=the item needs some revision

3=the item is clear but need some minor revision

4=the item is very clear

PLACE:

DATE:

VALIDATED BY:

☐ **PHYSICIAN**

☐ **PROFESSOR**

☐ **CLINICAL PHARMACIST**

Figure 1: Validation form.

Frequency of adverse drug reaction assessed by hartwig and siegel severity scale

The Severity of the reaction was classified based on Hartwig and Siegel severity assessment scale, in that majority of the reactions were observed under Moderate (55.81%) category (Figure 13).

Frequency of adverse drug reaction assessed by schumock and thornton preventability scale

The Preventability of the reaction was classified based on Schumock and Thornton preventability scale, in that majority of the reactions were observed under Probably Preventable (65.11%) category (Figure 14).

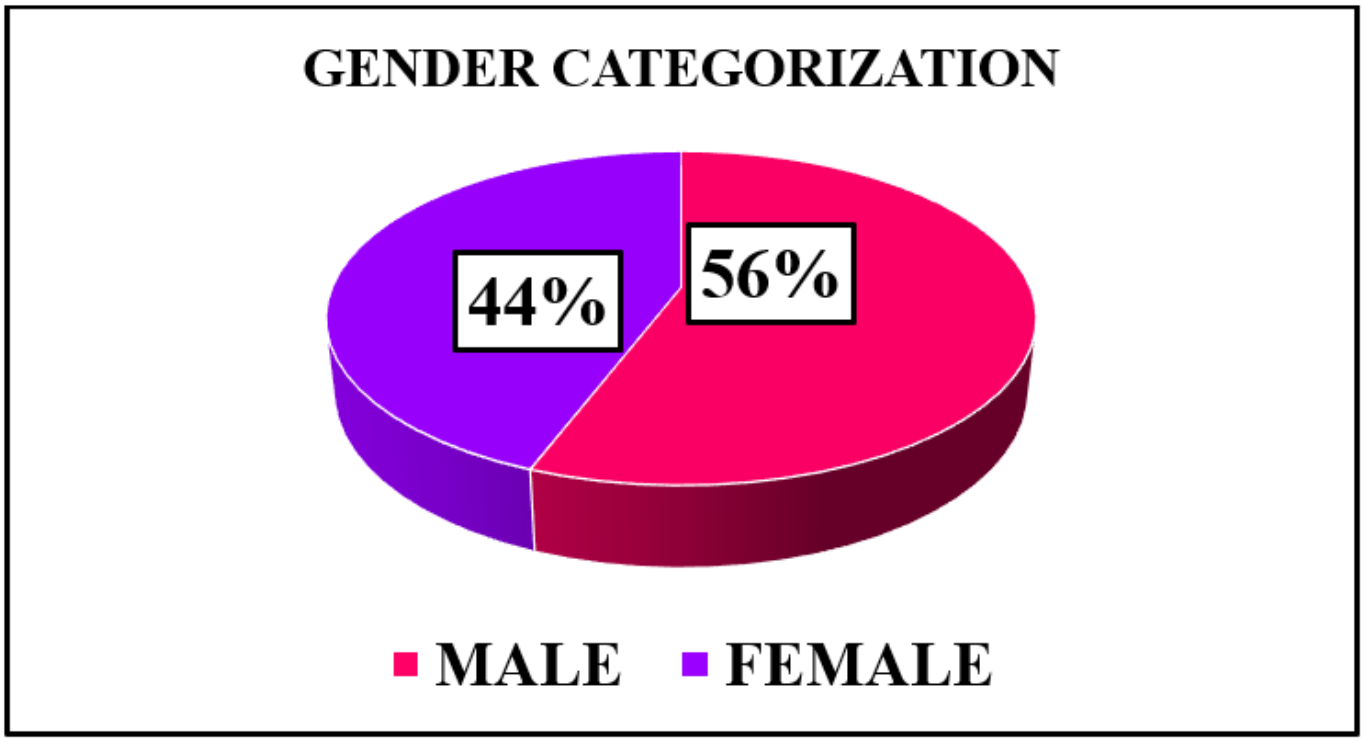


Figure 2: Gender wise distribution of patients (*n*=43).

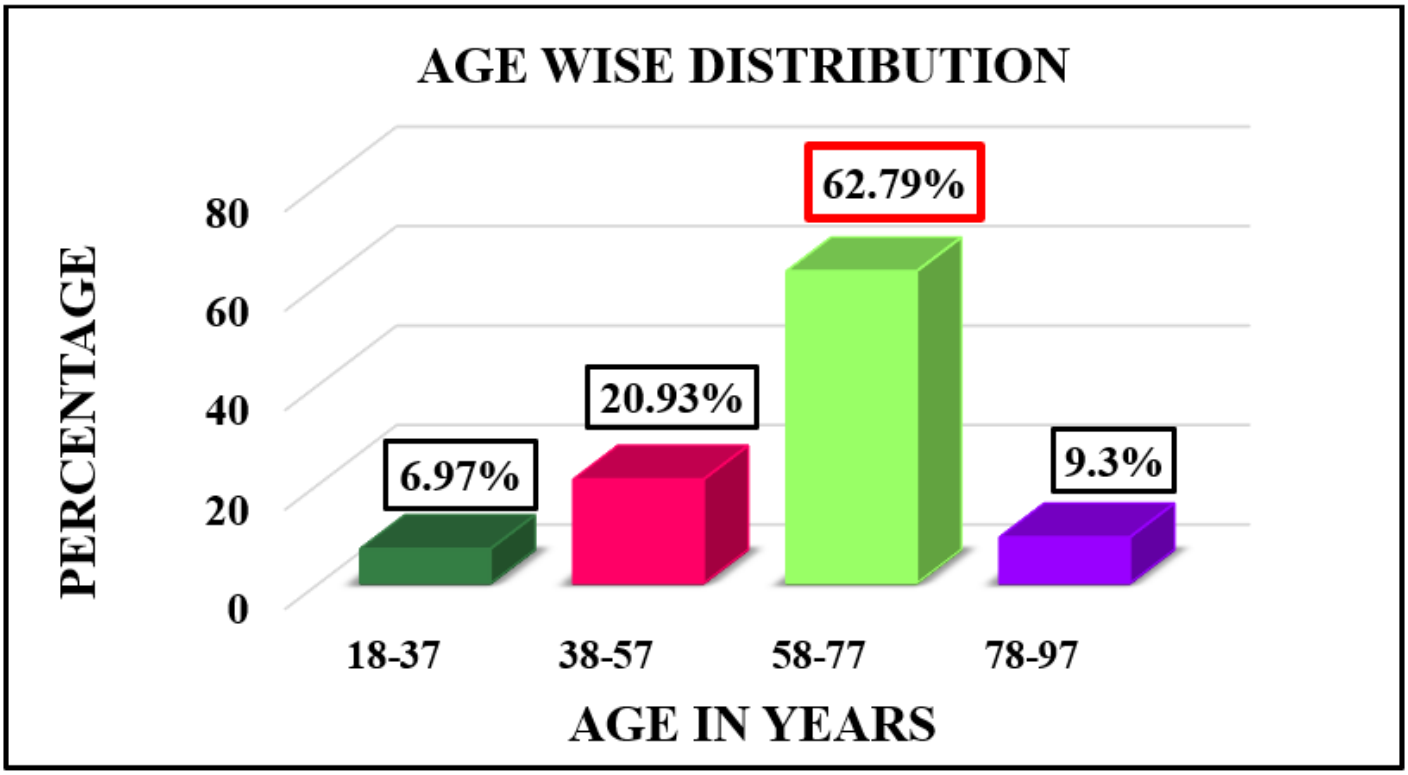


Figure 3: Age wise distribution of patients.

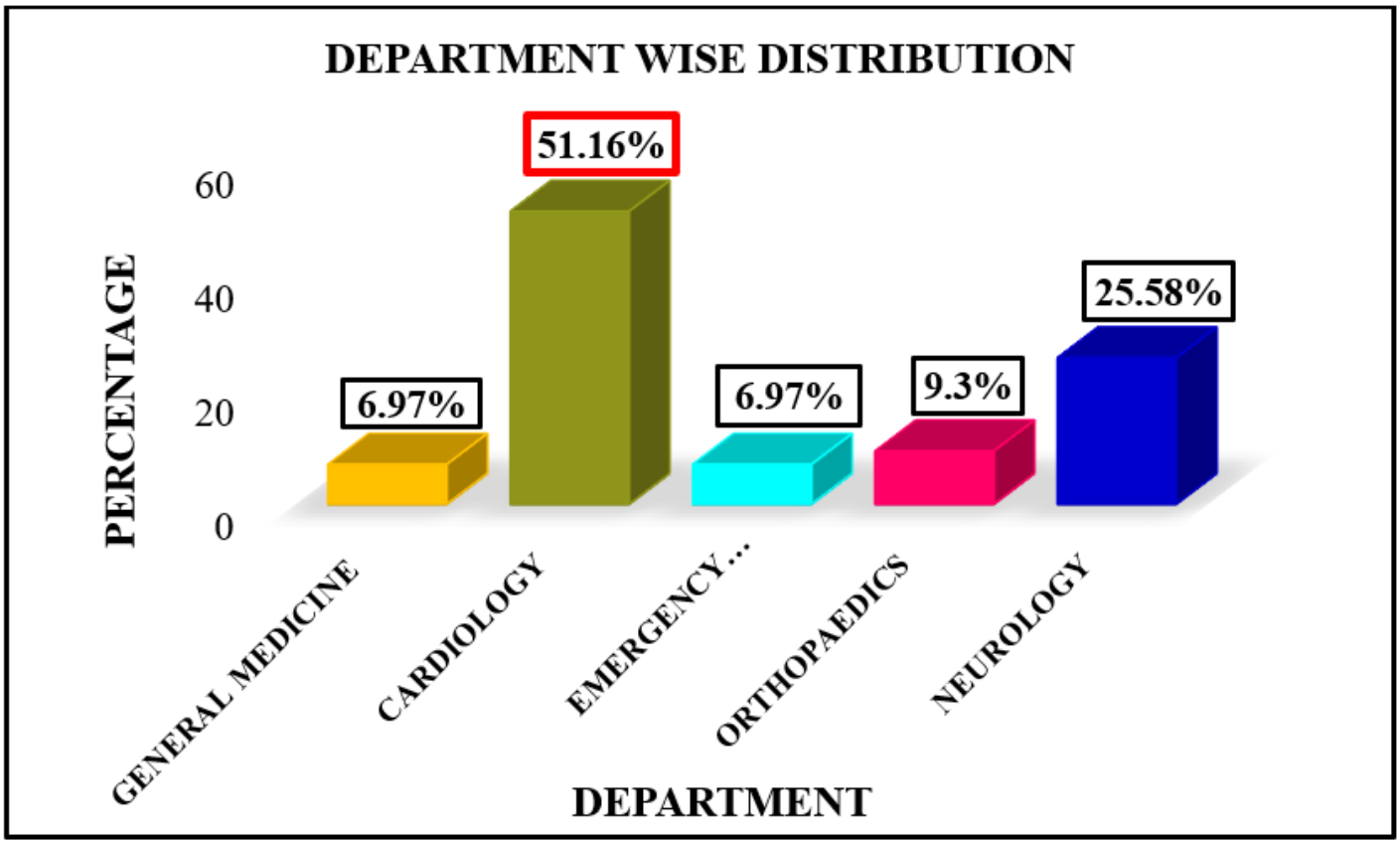


Figure 4: Department wise distribution of patients.

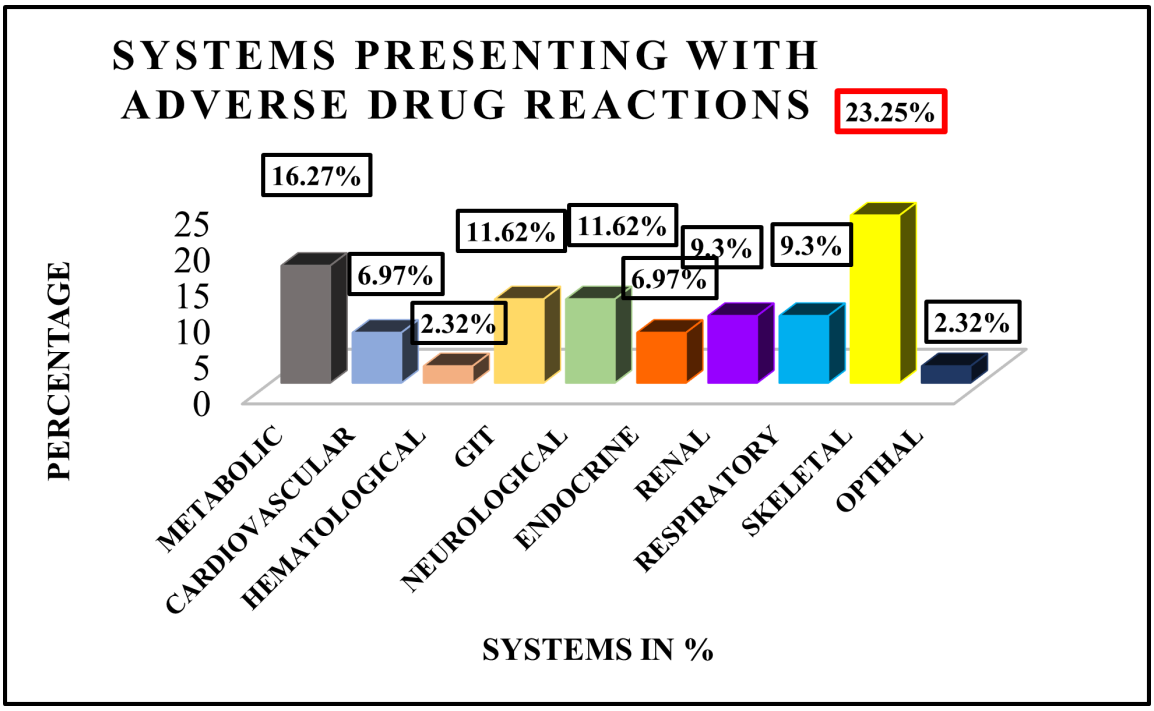


Figure 5: Systems presenting with adverse drug reactions.

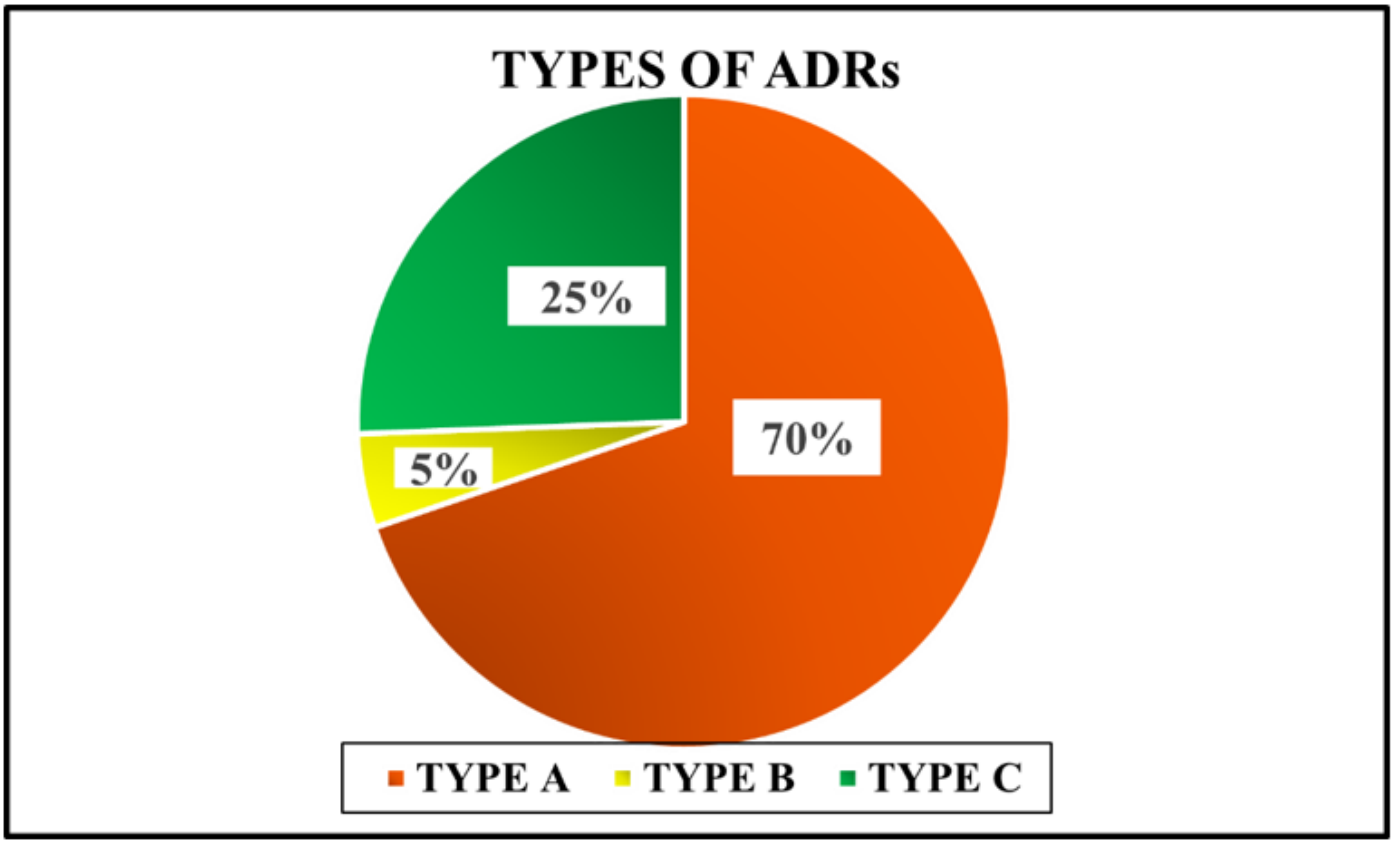


Figure 6: Frequency of types of adverse drug reaction.

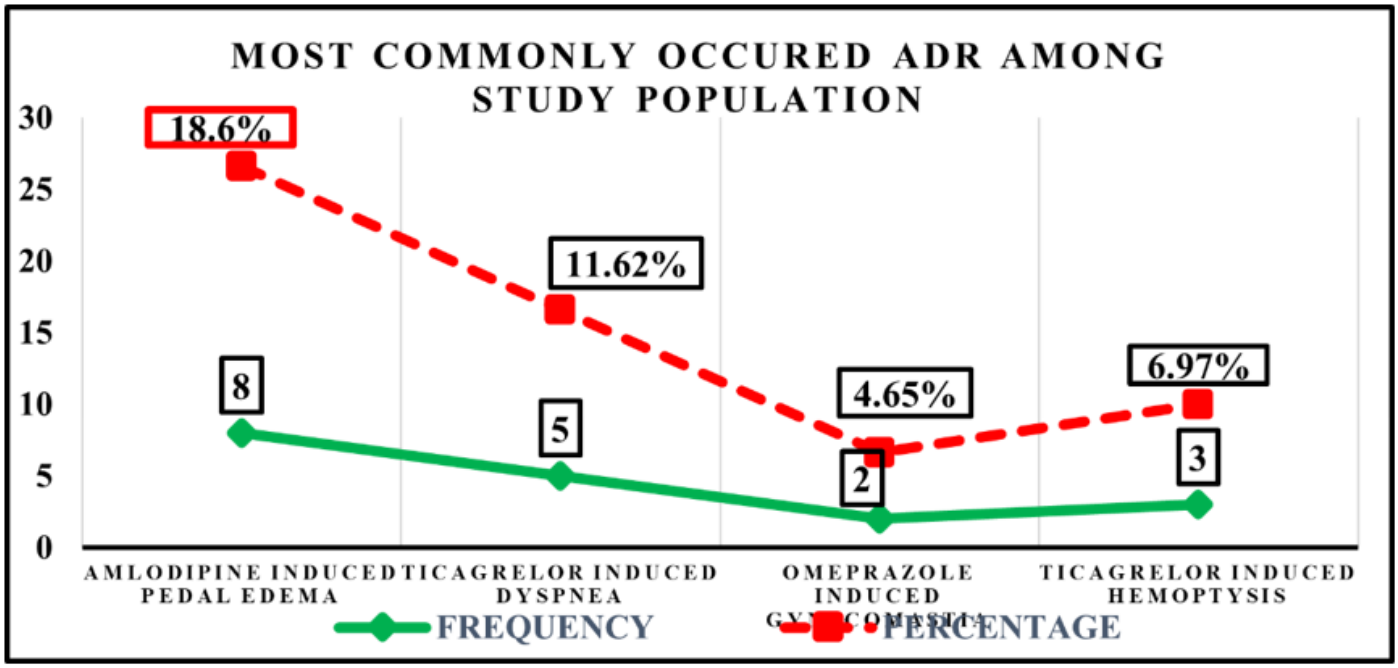


Figure 7: Frequency of most commonly occurred adverse drug reaction.

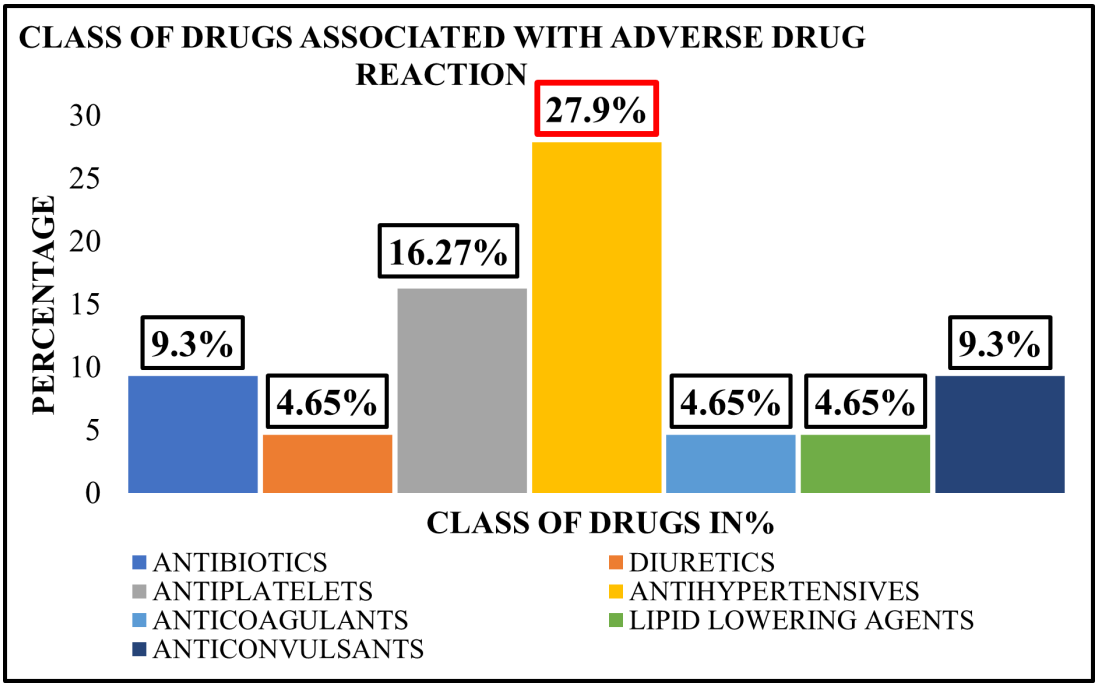


Figure 8: Frequency of class of drugs associated with adverse drug reaction.

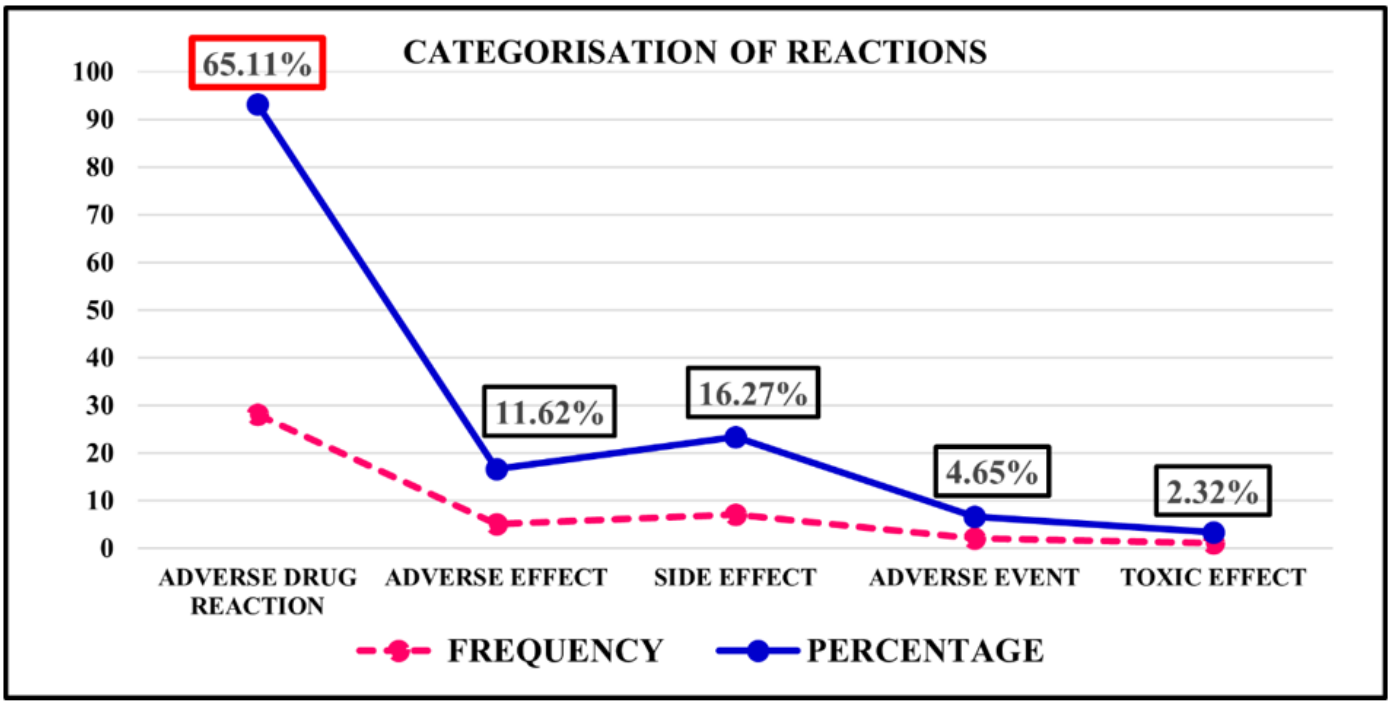


Figure 9: Frequency of categorization of reaction.

Frequency of adverse drug reaction assessed by liverpool avoidability scale

The Avoidability of the reaction was classified based on Liverpool Avoidability scale, in that majority of the reactions were observed under Possibly Avoidable (65.11%) category (Figure 15).

Frequency of adverse drug reaction assessed by svcp adr assessment scale

The Adverse drug reaction was classified based on SVCP ADR assessment scales, in that majority of the reactions were observed under Possibly Manageable (76.74%) category (Figure 16).

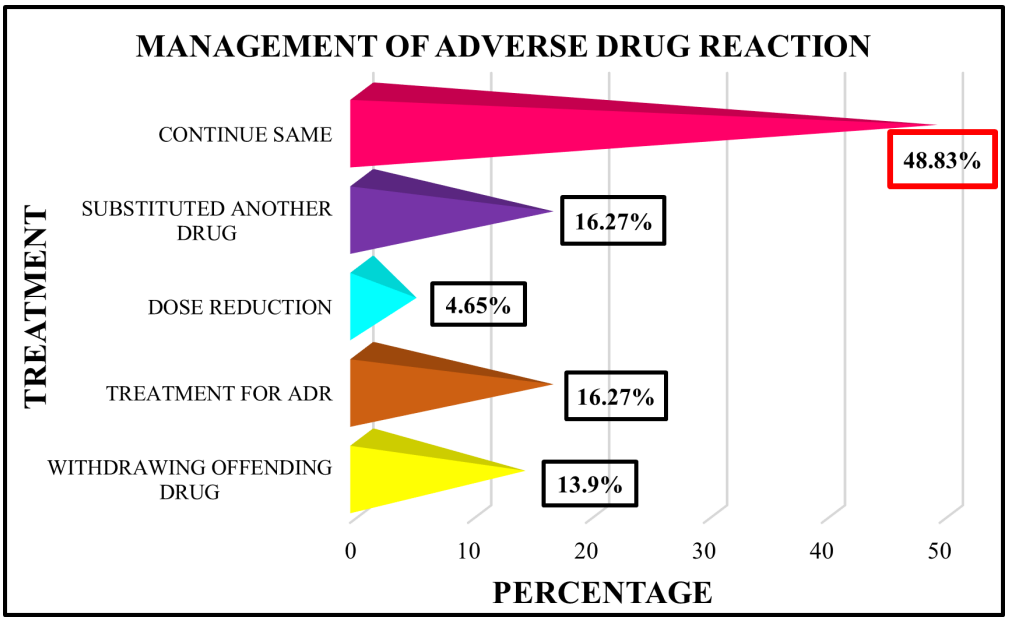


Figure 10: Frequency of management of adverse drug reaction.

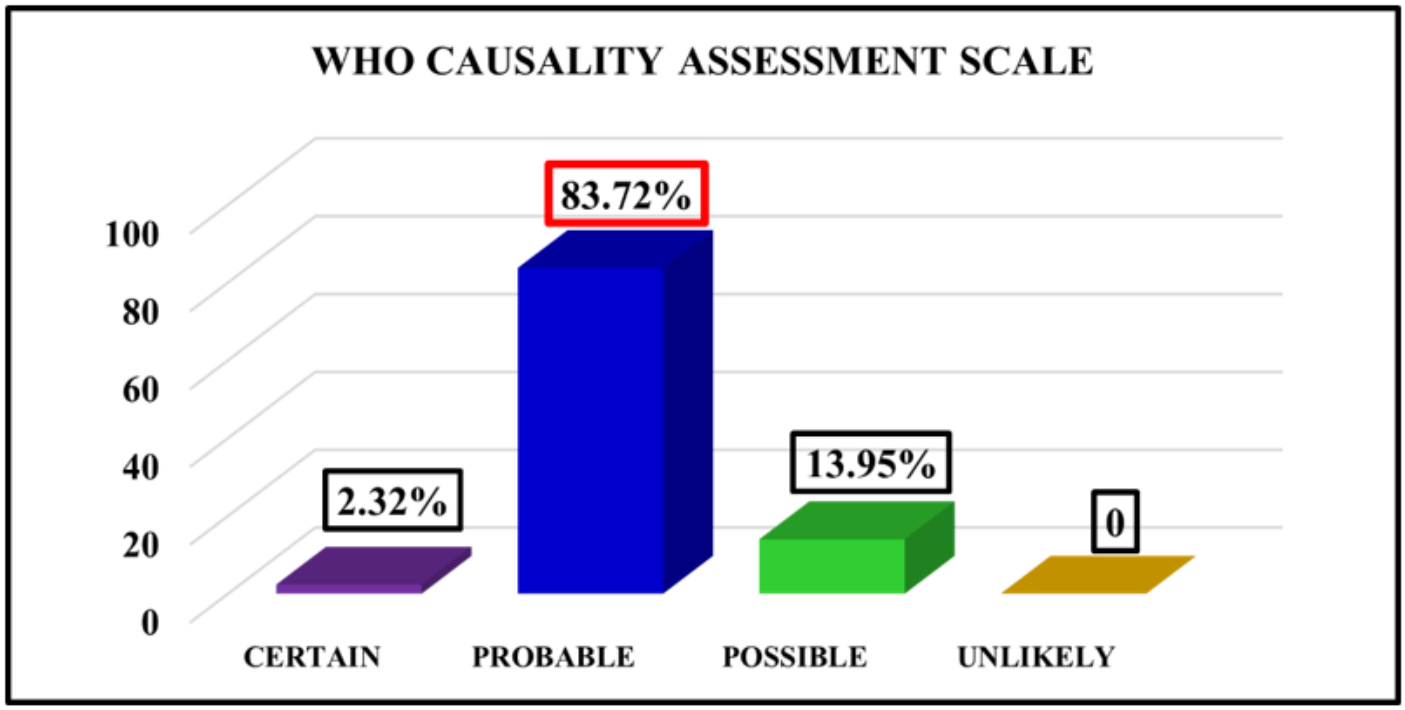


Figure 11: Frequency of adverse drug reaction assessed by WHO scale.

Frequency of adverse drug reaction by overall comparison of scales

The overall adverse drug reactions occurred among the study population were categorized and compared by means of SVCP ADR assessment scale with the other five ADR assessment scales. (Table 4) (Figure 17).

DISCUSSION

Adverse drug reactions constitute a significant risk to patient safety and can lead to substantial consequences for both patients and healthcare systems, impacting medical outcomes and economic factors. The study was conducted to detect adverse drug reactions among the study population by creating a novel assessment tool for ADRs. This tool was subsequently validated and compared against five other ADR assessment scales.

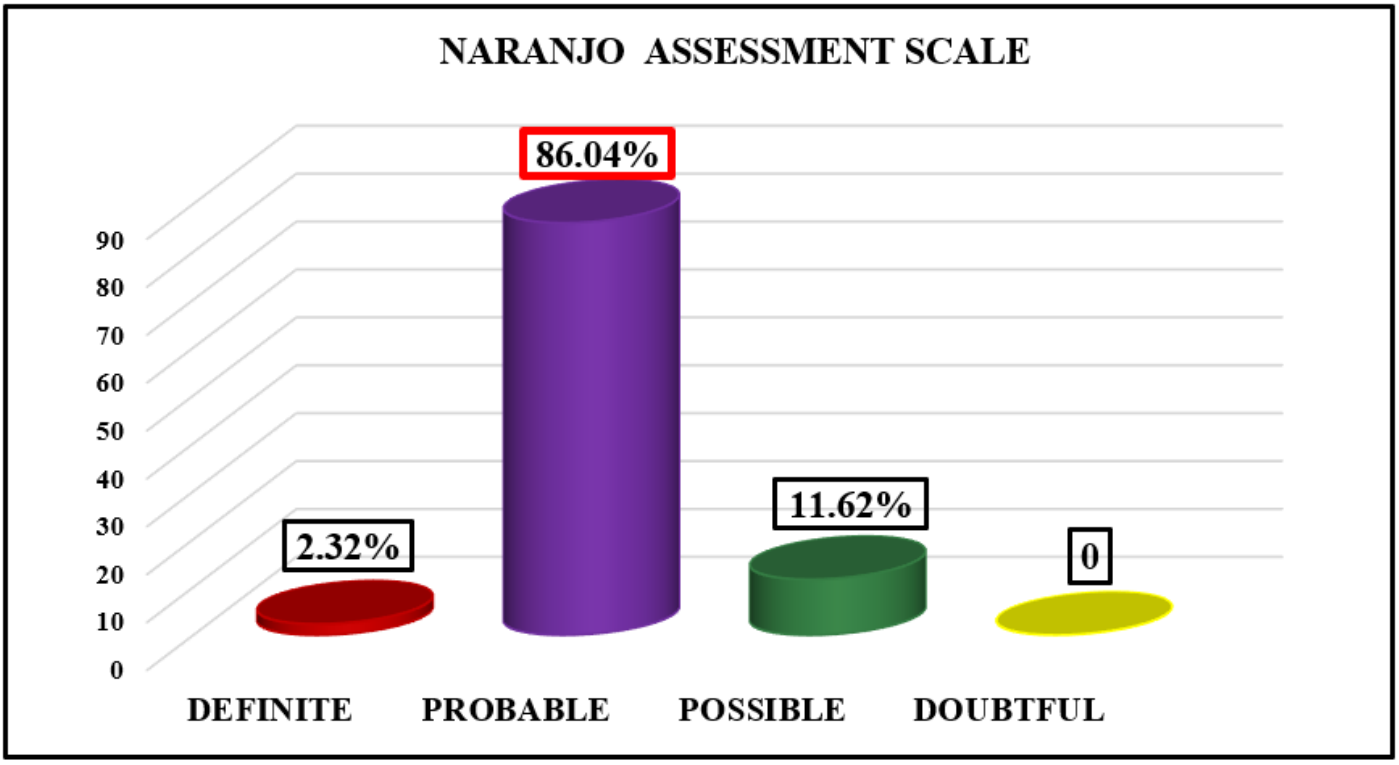


Figure 12: Frequency of adverse drug reaction assessed by Naranjo algorithm scale.

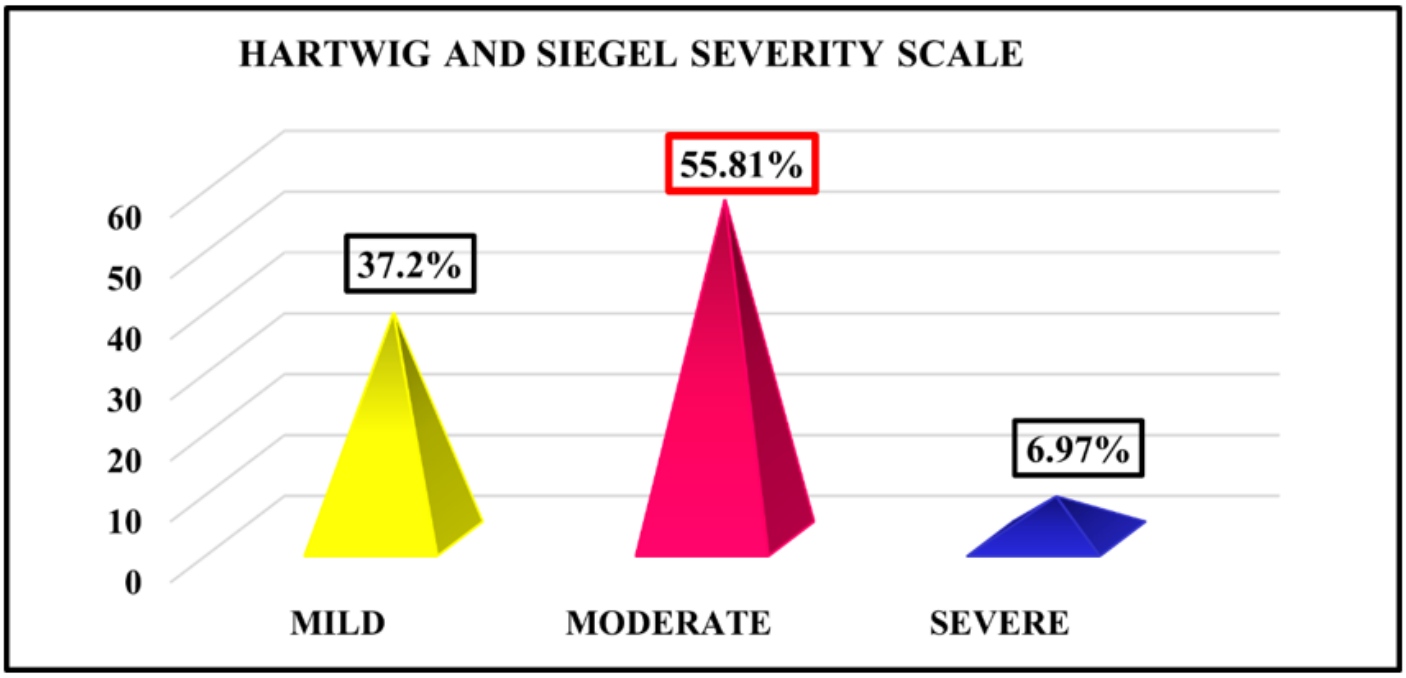


Figure 13: Frequency of ADR assessed by Hartwig and Siegel severity scale.

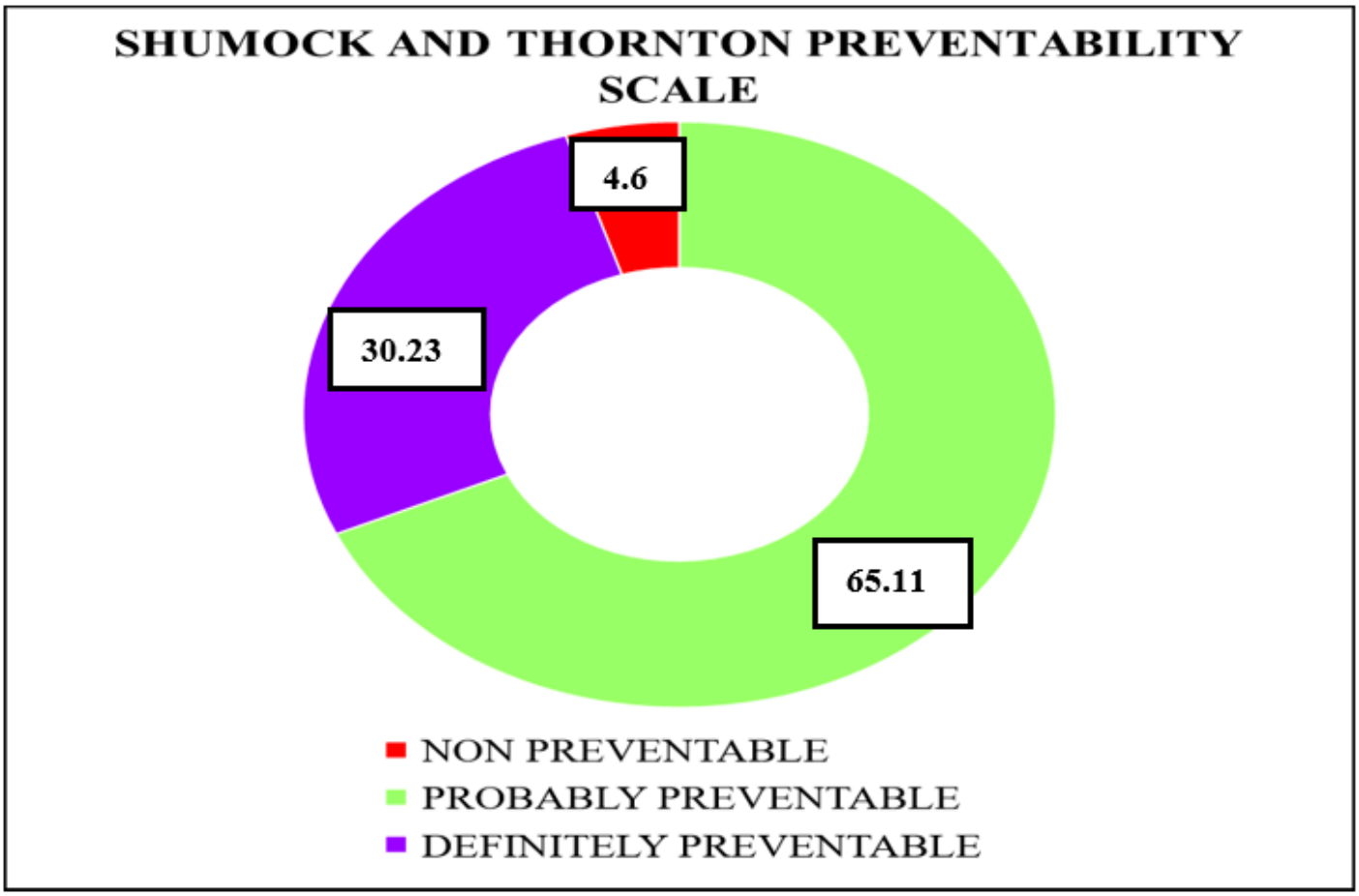


Figure 14: Frequency of adr assessed by Schumock and Thornton preventability scale.

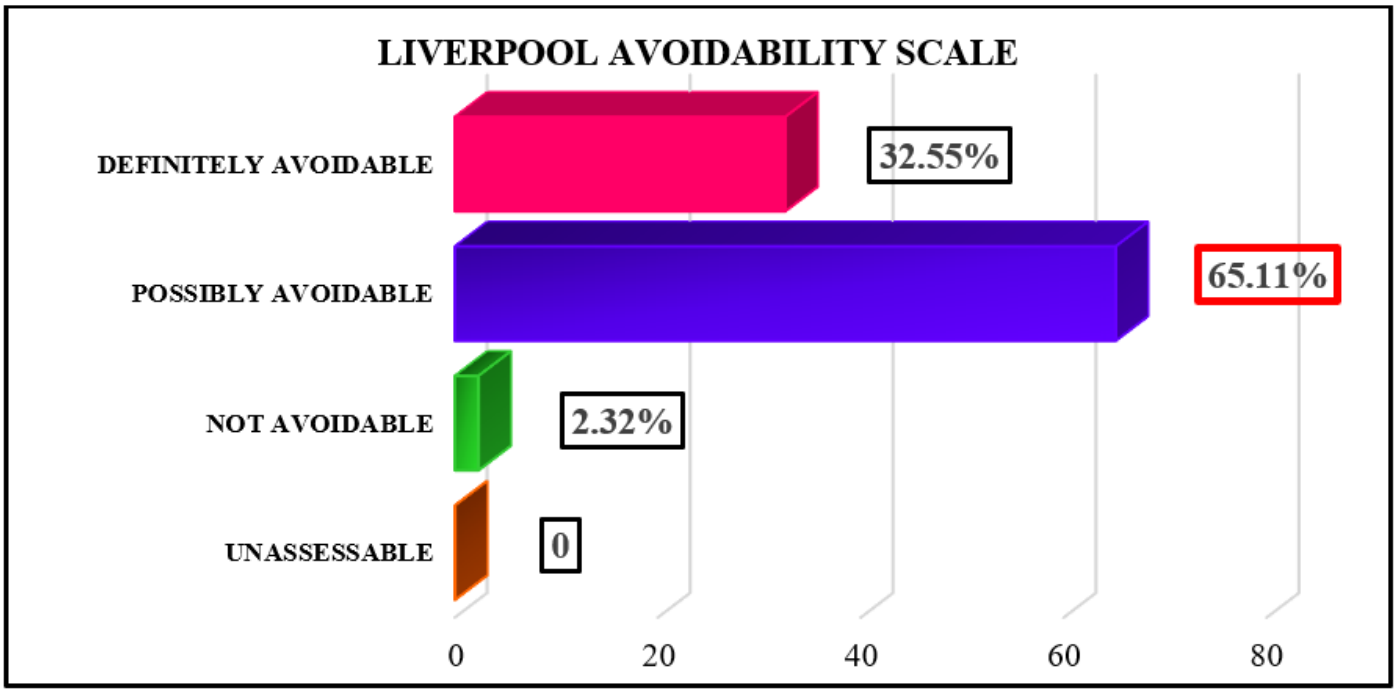


Figure 15: Frequency of adverse drug reaction assessed by Liverpool Avoidability scale.

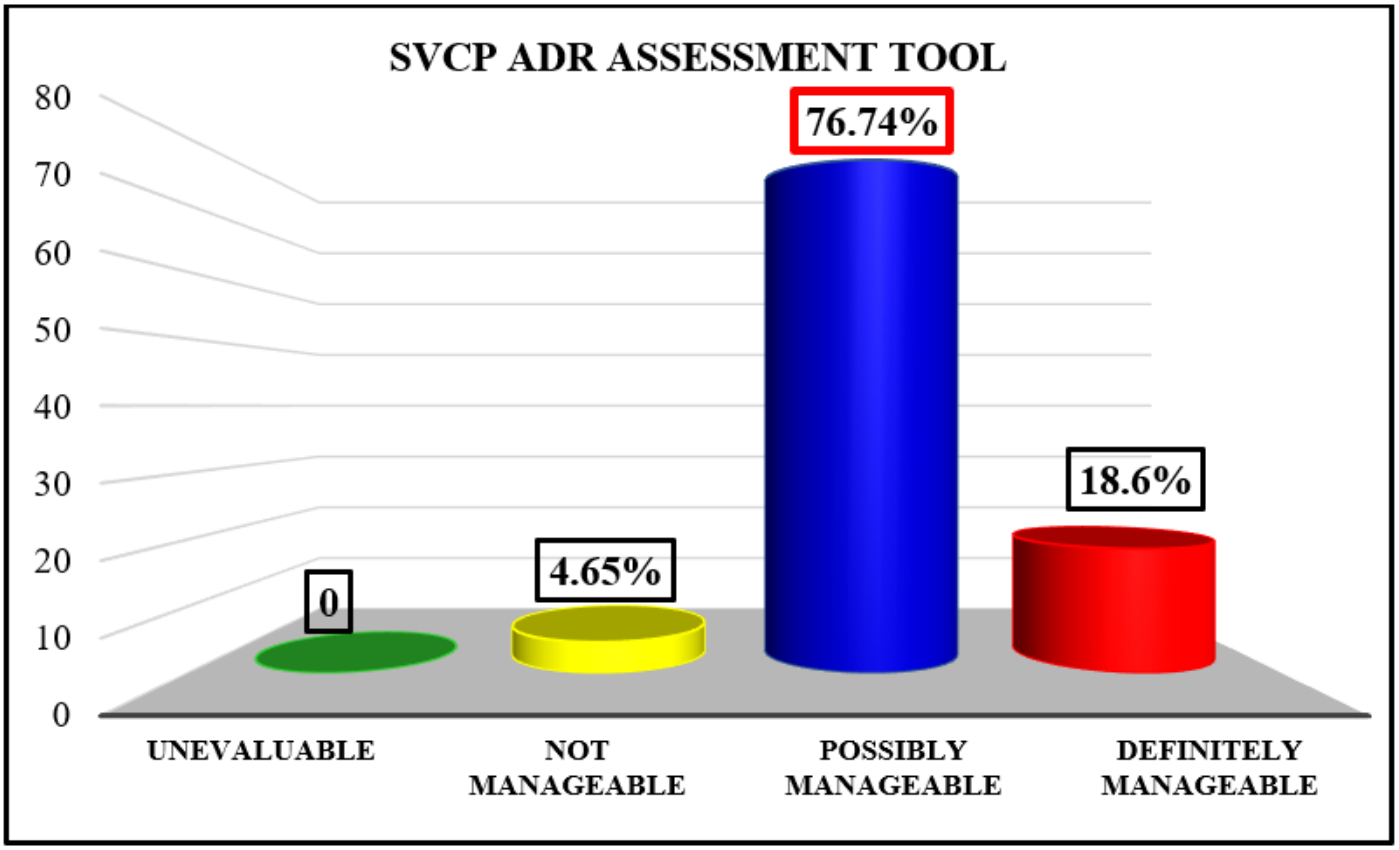


Figure 16: Frequency of adverse drug reaction assessed by SVCP ADR assessment scale.

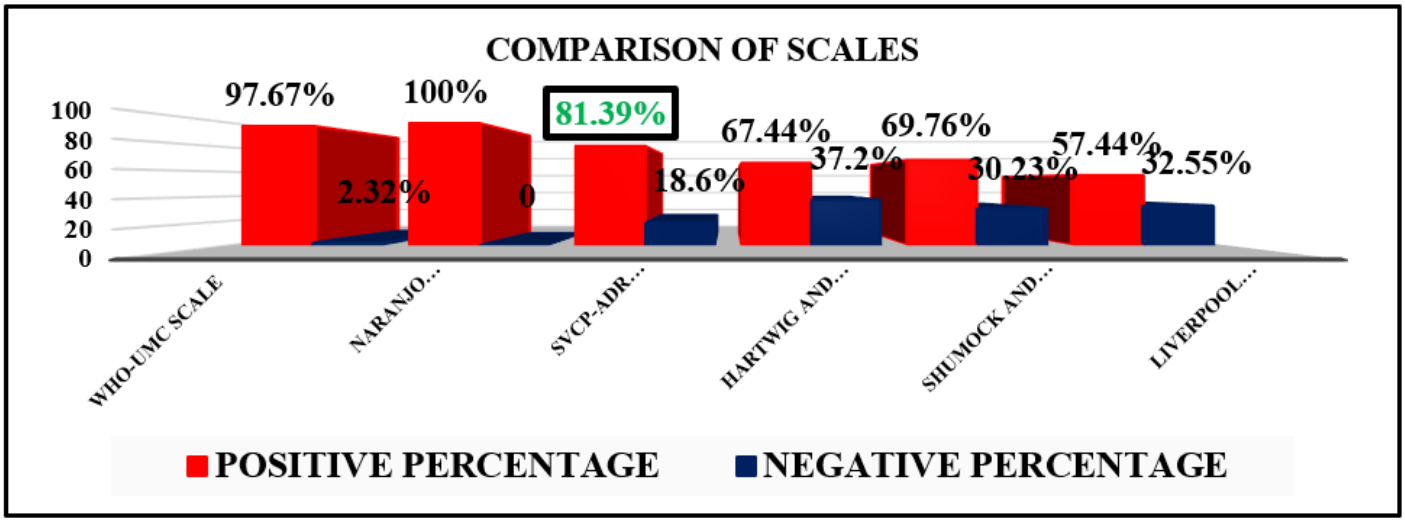


Figure 17: Frequency of adverse drug reaction by overall comparison of scales.

The validation of the SVCP-ADR assessment tool was carried out, as evident in the research conducted by Muhamad Saiful Bahri Yusof. Based on the inclusion and exclusion criteria of the study, 43 patients identified with ADRs were selected, which constituted 56% males and 44% females. 62.79% of the subjects predominantly belonged to the middle adulthood group of (58-77) years. Categorizing adverse drug reactions by department revealed that the Cardiology department (51.16%) had a higher incidence rate of ADRs. The most frequent system presenting with adverse drug reactions were skeletal system (23.25%) and this was categorized based on the study done by *Amee D Pandya, et al.*

In a study conducted by Yerramilli A, *et al.*, the majority of the reactions were categorized as Type A, with a significant portion of these reactions occurring in relation to antibiotics. However, in this study, the majority of the reactions fell into Type A (70%) and the major reactions were associated with antihypertensive medications. Within the study population, the most commonly

Table 4: Classification of positive and negative outcomes of various scales.

Outcome	Positive	Negative
Who-umc scale	Certain Probable Possible	Unlikely/unclassified Unassessable
Naranjo algorithm scale	Definite probable possible	Unlikely/Doubtful
Hartwig and siegel severity scale	Moderate Severe	Mild
Shumock and thornton preventability scale	Non-preventable probably preventable	Definitely preventable
Liverpool avoidability scale	Not avoidable possibly avoidable	Unassessable definitely avoidable
Svcp-adr assessment scale	Not manageable possibly manageable	Unevaluable definitely manageable

categorized and reported occurrences were adverse drug reactions, accounting for 65.11% of the cases, followed by side effects, which constituted 16.27% of the reported occurrences.

In a study conducted by Sung Ho Um, *et al.*, the outcomes assessed using the scales were divided into positive and negative outcomes to facilitate the comparison of the two scales. In this study, following the approach of that study, the outcomes evaluated using the six scales were classified into positive and negative outcomes for the purpose of comparing the SVCP-ADR assessment scale with the other five scales. The findings revealed that the SVCP-ADR assessment scale exhibited a higher number of positive outcomes compared to three of those scales.

Limitation

Because of the constrained timeframe, only a limited validation was performed. Therefore, it needs additional validation and certainty of results by experts. Additionally, we have intentions to create a mobile application that is software-based.

CONCLUSION

In this study, a tool was created and validated with a content validity index of 0.9 to facilitate the evaluation of adverse drug reactions. Furthermore, the results obtained from the five scales such as WHO causality assessment scale, Naranjo Probability scale, Hartwig and Siegel severity scale, Schumock and Thornton scale, Liverpool Avoidability scale were divided into positive and negative outcomes and these outcomes were compared with the SVCP-ADR assessment tool.

The study revealed a notable increase in positive outcomes in our tool when compared with the other three scales such as Hartwig and Siegel severity scale, Schumock and Thornton scale, Liverpool Avoidability scale. The newly developed tool is anticipated to achieve a generally favourable level of usability among healthcare professionals. Moreover, it is expected to make a valuable contribution to future research on adverse drug reactions, thereby enhancing drug safety efforts. This study can provide insight for Clinical Pharmacists (CP) in enhancing the detection and subsequent reporting of adverse drug reactions, thereby enhancing patient safety.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

ABBREVIATIONS

ADR: Adverse Drug Reaction; **SVCP:** Swamy Vivekanandha College of Pharmacy; **WHO:** World Health Organization; **CVI:** Content Validity Index; **AVE:** Average; **I-CVI:** Item Content Validity Index; **S CVI:** Sum of Content Validity Index; **UA:** Universal Agreement.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

The study was carried out after taking permission from the Institutional Ethical Committee of Vivekanandha Medical Care Hospital, Elayampalayam. (Ref. No. EC/NEW/INIT/2021/1811).

The consent was taken from the patient to participate in the study.

SUMMARY

The study focused on identifying ADRs in the study population through the development and validation of a novel assessment tool called SVCP-ADR. Adverse drug reactions are inherent risks linked to the utilization of medications. The identification of adverse drug reactions has gained greater importance due to the introduction of numerous new medications over the past two to three decades. The WHO has taken substantial steps in this regard by establishing an international centre for monitoring adverse drug reactions in Uppsala, Sweden.

Various scales are employed for assessing adverse drug reactions, yet most of these scales come with their own advantages and drawbacks. The primary aim behind creating standardized methods for assessing adverse drug reactions is to establish dependable, consistent and validated data concerning the link between adverse reactions and suspected drugs. The research demonstrated a significant rise in favourable outcomes with our tool compared to three other scales: Hartwig and Siegel severity scale, Schumock and Thornton scale, Liverpool Avoidability scale. We anticipate our newly developed tool to be widely accepted and usable among healthcare practitioners. Furthermore, it's prepared to offer valuable insights for future studies on adverse drug reactions, thereby promoting drug safety initiatives. This study offers valuable guidance for Clinical Pharmacists in improving the identification and reporting of adverse drug reactions, consequently enhancing patient safety.

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