Precedence of Cognizant Adverse Drug Reactions (ADRs) Reporting in a South Indian Tertiary Care Hospital: A Prospective Study

Nimisha Raveendran[1], Sharath Kumar K[2], Mohandas Rai[3], Arun Ravindran[4,*], Chandrashekar R[5]

[1]Post Graduate/ Tutor, [2,4,5]Assistant Professor, [3]Professor & HOD, Dept. of Pharmacology, A.J. Institute of Medical Sciences & Research Centre, Karnataka

***Corresponding Author:**
Email: arunrav848@gmail.com

Abstract

Objectives: The present study was conducted with the objectives to analyze the ADRs reported to the ADR Monitoring Centre at a tertiary care hospital in Dakshina Kannada district, South India.

Methods: Adverse drug reaction (ADRs) reports were collected over a span of two years for assessing an agreement between two causality assessment tools; WHO-UMC criteria and Naranjo algorithm.

Results: There were 30 (46%) males and 36 (54%) females reported which were categorized into Type A (Augmented) and Type B (Bizarre) ADRs having 24 (36.4%) and 42 (63.6%), respectively, based on Modified Rawlins and Thompson Scale where majority of cases were 'Probable', followed by 'Possible' categories. Criteria for avoidability were determined to be 44(66.7%) as Not avoidable and 22 (33.3%) as possibly avoidable. Severity of ADRs were determined to be 54(81.8%) for moderate, and 6 (9.1%) for each of mild and severe categories. Amongst the drug classes concerned, 28 (42.4%) cases were attributed to Anti-infective followed by Anti-Diabetic and Radiocontrast Media constituting 18(27.3%) and 7(10.6%) cases respectively. Cephalosporins were the most common class of drugs associated with ADRs constituting 16 (24.2%) cases. Kappa test was utilized to assess the comparison of agreement between the two causality assessment criteria of WHO-UMC scale and Naranjo Algorithm and the value was 0.2.

Conclusions: This study is indicative of 'poor' agreement between the two widely used criteria of WHO-UMC scale and Naranjo Algorithm.

Keywords: Adverse drug reactions, Precedence, Reporting.

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Introduction

Adverse Drug Reactions (ADRs), have a considerable prevalence in the healthcare setting. A meta-analysis done in 2002 showed that 4.9% of hospital admissions are associated with ADRs, with the prevalence ranging between 0.2 to 41.3% in individual studies1. ADRs also impose a substantial economic burden on society via various aspects, such as costs and loss of productivity[1,2]. Data suggests that, among both outpatients as well as inpatients, almost half of the ADRs reported were preventable. The global threat posed by ADRs is being tackled via the application of Pharmacovigilance[3].

World Health Organization (WHO) defines Pharmacovigilance as 'The science and activities related to the detection, assessment, understanding and prevention of adverse effects or any other possible drug related problems[4]. Over the years, Pharmacovigilance has evolved and taken a broader stance; monitoring both pre-marketing and post-marketing phases of a medicinal product's life cycle[5]. Presently, under the aegis of the government; the Pharmacovigilance Programme of India (PvPI) has taken up the onus of ADR monitoring in the nation. As part of this initiative, various PvPI recognized ADR monitoring centers (AMCs) from across India, are constantly monitoring and reporting drug related adverse events, thus collectively working towards the common goal of drug safety[6]. While measures should be taken to address this; it is also imperative to analyze the reported ADR data thoroughly, as this information is valuable in detecting patterns of adverse events at the AMC and regional levels. When analyzing an ADR, the establishment of a causal relationship between the suspected drug and the event is particularly essential. Two of the most common tools used for causality assessment are, the World Health Organization Collaborating Centre for International Drug Monitoring - Uppsala Monitoring Centre Criteria (WHO–UMC criteria) and the Naranjo Probability Scale/Algorithm[7,8]. As both scales are widely popular, it is important to assess the agreeability of results when utilizing them for assessing an ADR report[9,10].

Hence, the present study was conducted with the objectives of analyzing the ADRs reported to the ADR Monitoring Centre at a tertiary care hospital in Dakshina Kannada district, South India over a span of two years (Jan 2013-Dec 2015) and to assess the agreement between two causality assessment tools; WHO-UMC criteria and Naranjo algorithm.

Materials and Methodology

Ethical clearance was obtained from the Institutional ethics committee, A.J. Institute of Medical Sciences and Research Centre, Mangalore, Karnataka, India.

Study Design

A descriptive and comparative analysis of all ADRs reported to the ADR Monitoring Centre (AMC) at A.J. Institute of Medical Sciences and Research Centre (AJIMS & RC) was conducted. This data was obtained from information of ADRs collected using Central Drug Standard Control Organization (CDSCO) ADR reporting forms, over a period of two years (Jan 2013-Dec 2015) from various departments of A.J. Institute of Medical Sciences and Research Centre, Mangalore, Karnataka, India. A universal sampling technique was utilized here.

Study Procedure

A total of 66 ADR reports were obtained over a span of two years (Jan 2013-Dec 2015) and were analyzed as per the following criteria

- Demographic details of patients (Age and Sex)
- Types of ADRs – using Modified Rawlins and Thompson classification
- Causality assessments - using WHO – UMC causality assessment criteria and Naranjo algorithm
- Avoidability of ADRs - using Hallas criteria for avoidability
- Severity of ADRs – using Modified Hartwig and Siegel Scale
- Organ system involved – using World Health Organization – Adverse Reaction Terminology (WHO-ART) system organ class sorting
- Class of drugs implicated
- The evaluations of the ADRs were carried out by one of the authors who had an experience in the field of Pharmacovigilance. Subsequently, the comparison of the causality of the ADRs, obtained using WHO – UMC criteria and Naranjo algorithm was performed by the same author.

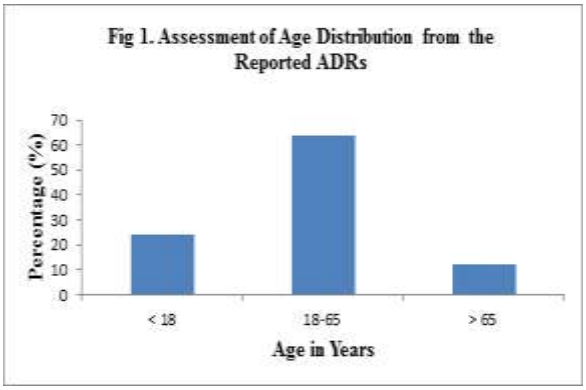
Statistical Analysis

Descriptive analysis of the compiled ADR reports was expressed as percentages of the total observations. Assessment of comparison between the causality assessment criteria was carried out using Kappa's test. SPSS version 18 was used for the analysis.

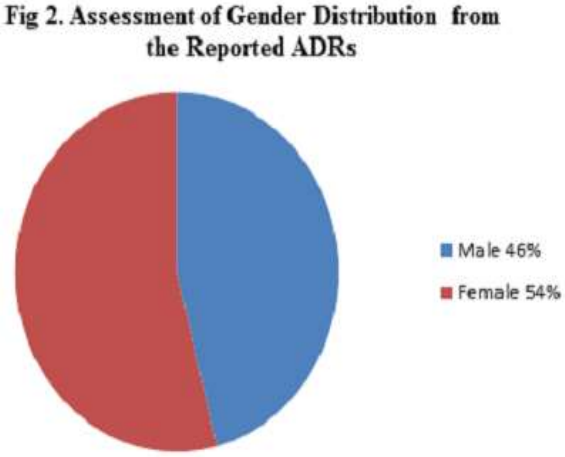
Results

Demographic details

Age Distribution: The age distribution of the patients, in whom ADRs were reported, was found to be 24.2%, 63.6% and 12.1% in age groups of less than 18 years, 18 – 65 years and more than 65 years, respectively (Fig. 1).

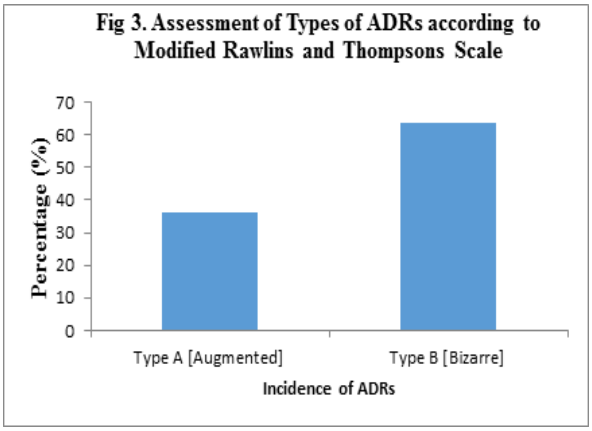


Gender Distribution: There were 30 (46%) and 36 (54%) females reported to have suffered ADRs in our study (Fig. 2).



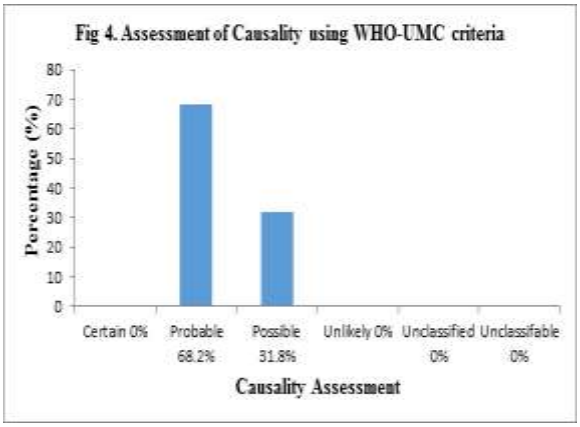
Types of ADRs

ADRs were categorized into Type A (Augmented) and Type B (Bizarre) having 24 (36.4%) and 42 (63.6%), respectively, based on Modified Rawlins and Thompson Scale. (Fig 3).

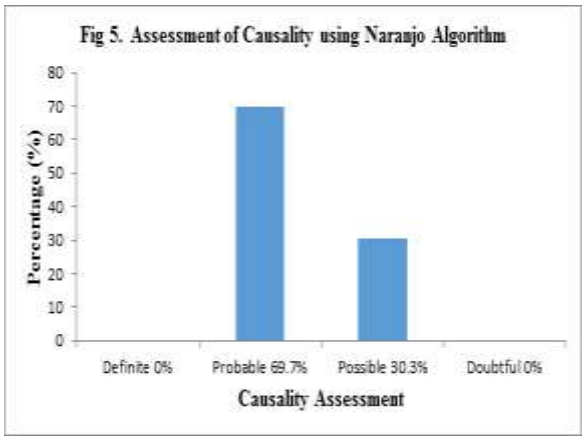


Causality Assessments according to WHO – UMC causality assessment criteria: Causality of the ADRs using this scale was classified into Certain, Probable,

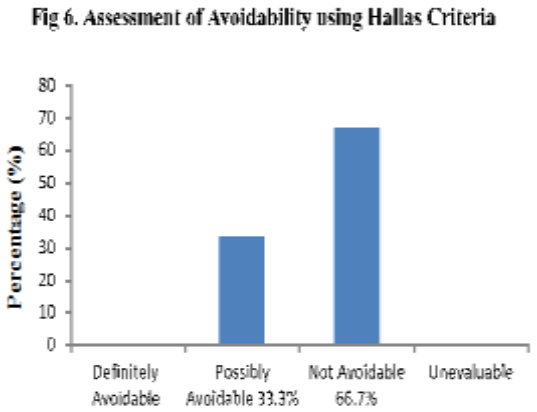
Possible, Unlikely, Unclassified and Unclassifiable. There were 45 (68.2%) Probable cases and 21(31.8%) Possible cases (Fig. 4).



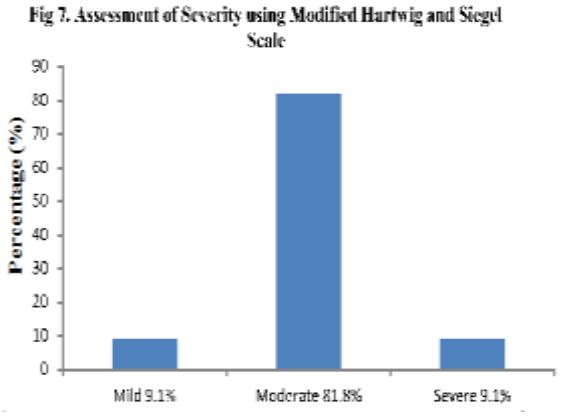
Causality Assessments according to Naranjo Algorithm: Causality of ADRs using Naranjo Algorithm was assessed and categorized as Definite, Probable, Possible and Doubtful. There were 46 (69.7%) Probable cases and 20 (30.3%) Possible cases (Fig. 5).



Assessment of Avoidability of ADRs according to Hallas criteria: Hallas criteria for avoidability categorizes ADRs into Definitely Avoidable, Possibly Avoidable, Not avoidable and Unevaluable. The ADRs obtained were determined to be 44 (66.7%) Not avoidable and 22 (33.3%) Possibly Avoidable. There were no definitely avoidable or Unevaluable ADRs (Fig. 6).

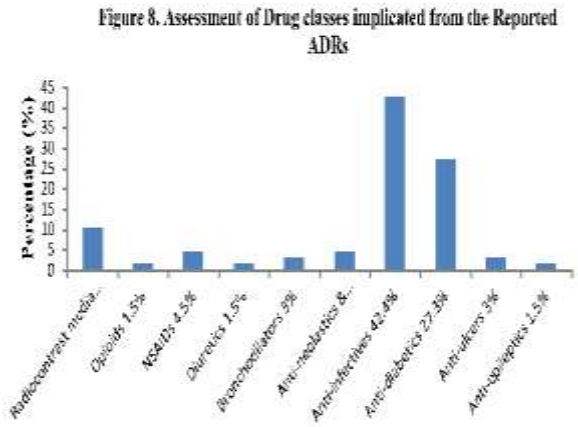


Assessment of Severity of ADRs using Modified Hartwig and Siegel Scale: Assessment of Severity of ADRs using Modified Hartwig and Siegel Scale assigns ADRs into Mild, Moderate and Severe portfolio. Moderate cases were determined to be 54 (81.8%) while there were 6 (9.1%) cases each of mild and severe categories (Fig. 7).



Organ System Involved according to WHO-ART system: WHO-ART system organ class sorted the majority of the ADR cases into those with involvement of Skin and appendages 28 (42.4%) and Endocrine system 16 (24.2%) mainly. Among these, Maculopapular Rashes (33.3%) and Hypoglycemic Episodes (24.2%) were the most common reported events.

Classes of drugs implicated: Amongst the drug classes concerned, majority of the cases were attributed to Anti-infectives 28 (42.4%), Anti-Diabetic 18 (27.3%) and Radiocontrast Media 7 (10.6%). Cephalosporins 16 (24.2%) were the most common class of drugs associated with ADRs (Fig. 8).



Comparison of the Causality Assessment Criteria according to WHO-UMC scale and Naranjo Algorithm: Kappa test was utilized to assess the comparison of agreement between the two causality assessment criteria WHO-UMC scale and Naranjo Algorithm. The value was determined to be 0.2.

Discussion

Causality assessment is used to determine the likelihood that a drug caused a suspected ADR. There are a number of different standard algorithms used to judge causation, including Naranjo algorithm, WHO-UMC scale, Kramer algorithm etc. Each of the tools have their pros and cons, and subjectivity of assessment is important in their use. There are multiple factors to be considered when assessing ADRs such as the chronology of the event, co-prescribed medications, co-morbid conditions etc.[11,12]. Assigning causality to a specific agent is often a difficult task, especially considering accuracy of results. Psychiatric ADRs are often missed as they are grouped together in the questionnaires used to assess the population[13,14].

The age distribution of the patients in our study, in whom ADRs were reported, was found to be 24.2%, 63.6% and 12.1% in age groups of less than 18 years, 18 – 65 years and more than 65 years, respectively which shows the importance of age group experiencing the ADRs in hospital setting (Fig. 1). There were 30 (46%) males and 36(54%) females reported to have reported with ADRs in our study (Fig. 2). ADRs were categorized into Type A (Augmented) and Type B (Bizarre) having 24 (36.4%) and 42 (63.6%), respectively based on Modified Rawlins and Thompson Scale (Fig. 3). There were 45(68.2%) Probable cases and 21(31.8%) Possible cases (Fig. 4) according to WHO-UMC causality assessment criteria and (69.7%) probable and (30.3%) possible according to Naranjo Alogrithm, indicating variability in the results obtained (Fig. 4 & 5).

Criteria for avoidability were determined to be 44 (66.7%) as Not avoidable and 22 (33.3%) Possible avoidable (Fig 6). This pressurizes the importance of reporting ADRs which might result in reduction of ADRs. Assessment of Severity of ADRs was 54 (81.8%) constituting moderate, while there were 6 (9.1%) cases each of severe and mild categories (Fig. 7). WHO-ART system organ class sorted the majority of the ADR cases into those with involvement of Skin and appendages 28 (42.4%) and Endocrine system 16 (24.2%) mainly. Among these, Maculopapular Rashes (33.3%) and Hypoglycemic Episodes (24.2%) were the most common reported events. Amongst the drug classes concerned, 28 (42.4%) cases were attributed to Anti-infectives followed by Anti-Diabetic and Radiocontrast Media constituting 18 (27.3%) and 7 (10.6%) respectively. Cephalosporins were the most common class of drugs associated with ADRs constituting 16 (24.2%) cases (Fig. 8).

The prevalence of ADRs associated with commonly used drugs such as Cephalosporins seen in our study, highlights the requirement for a wider gamut for ADR monitoring. This will ensure that even incognito ADRs shall be identified. When we applied Kappa test to assess the comparison of agreement between the two causality assessment criteria WHO-UMC scale and Naranjo Algorithm, the value was determined to be 0.2 showing poor agreement.

The decision to assess whether an ADR can be attributed to a drug is often based on clinical judgment alone. To bring uniformity and reproducibility to this decision making process, causality assessment tools such as Naranjo algorithm and the WHO-UMC scale was developed. But studies have shown variability in the results obtained using these; even when two or more raters assessed the same set of ADRs.[16] The poor agreement shown between the two causality assessment tools in our study is corroborative with results seen in a previous study conducted elsewhere[15,16]. This shows the lacunae in the accuracy of results obtained using these different tools. The poor agreement shown in our study indicates the need for developing a universally acceptable standardized tool, reducing the ambiguity that prevails in the causality assessment of ADRs today.

Conclusion

Surveillance for ADRs needs to be strengthened, especially when prescribing anti-infective medications. The "fair agreement" noted between the Naranjo algorithm and the WHO-UMC scale in this study is indicative of lacunae in algorithms that needs to be addressed.

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