Review Article

Trigger Tool Based Detection of Adverse Drug Reactions in a Tertiary Care Teaching Hospital: A Prospective Observational Study

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ABSTRACT

Background: The use of "triggers" to identify Adverse Drug reactions (ADRs) is a novel emerging method for measuring the overall level of harm from medications in a health care organization. Our main objective is to determine the incidence of adverse drug reactions in the hospitalized patients and to compare Global Trigger Tool (GTT) with conventional method to identify ADRs. **Methodology:** A Prospective observational study was conducted over a period of six months during November 2016-April 2017. Modified Global Trigger Tool was used to identify triggers. 16 triggers were used to identify ADRs. Causality assessment of ADRs was done using Naranjo scale and severity and harm categorization of ADRs were assessed using NCC MERP. **Results:** A total of 244 patient profiles were analyzed. The results reveal that 193 triggers were identified in 125 patients and 93 ADRs were found in 81 patients. Out of which, 64 (68.81%) ADRs were found by triggers and 29(31.18%) ADRs were found spontaneously without the presence of a trigger. There is a remarkable improvement in the identification of ADRs using trigger tool in comparison to traditional approach. Of 93 ADRs identified, 69 (74.19%) were probable and 24 (25.81%) were possible. Similarly, 65 (69.89%) were determined to be NCC-MERP harm category E and 28 (30.11%) were category F. **Conclusion:** The study results suggest that IHI global trigger tool could be useful to identify ADRs in hospitals twice as more efficiently when compared to traditional ADR identification methods. It is an effective method to enable clinical pharmacists to identify ADRs and management of the same.

Key words: Adverse drug reactions (ADRs), IHI global trigger tool, NCC-MERP harm category, Causality, Prospective, Naranjo scale.

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INTRODUCTION

Adverse drug reactions (ADRs) are one of the leading causes of morbidity and mortality. It has been estimated that approximately 2.9%-5.6% of all hospital admissions are caused by ADRs and as 35% of the hospitalized patient's experience an ADR during their hospital stay.[1] ADR incidence has been reported in the range of 5.9 to 22.3% of all emergency department admissions in India. It has been reported that deaths due to ADRs contributed for 1.8% of total of deaths in India.[2] Early detection, evaluation and monitoring of ADRs are essential to reduce harm to patients and thereby improving public health.[3] The detection of ADRs has become increasingly significant because of the introduction of many newer medicines in the last two or three decades.

A trigger is defined as an occurrence, prompt or flag found on review of the medical record that "triggers "further investigation to determine the presence or absence of an adverse event".[4] A

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trigger may include laboratory trigger, medical trigger and clinician trigger. Earlier studies report that use of triggers promotes more focused chart review and thus may help to identify ADRs.[4-6] The Institute of Healthcare Improvement (IHI) simplified the manual patient case chart review process and developed the Global Trigger Tool (GTT) consisting of 19 triggers in order to monitor adverse events rates in a way that was easy to replicate in hospitals, with or without computerized records.[7]

Recent studies using the IHI Global Trigger Tool have identified harm rates in adults in US hospitals of 49 per 100 Admissions (33% of patients),[8] 36 per 100 admissions (28% of patients) in Medicare patients, 25 per 100 admissions (18% of patients) across North Carolina.[9] Till date, there are very few studies conducted in this area using trigger tool approach. Hence, our study aimed to study the assessment of ADRs using trigger tool approach and conventional method.

METHODOLOGY

Study design and Participants

This is a prospective observational study which was carried out for a period of 6 months (November 2016 to April 2017) in patients admitted to Dr. Pinnamaneni Siddhartha Institute of Medical Sciences and Research Foundation, which is an 850-bedded tertiary care teaching hospital at Chinaoutpalli, Gannavaram Mandal, Krishna district, Andhra Pradesh (India).

Ethical consideration

The study protocol (Number: PG/160/2017) was approved by Institutional Ethics Committee of Dr. Pinnamaneni Siddhartha Institute of Medical Sciences and Research Foundation (Dr. PSIMS and RF) which was registered with CDSCO (Reg. No: ECR/804/Inst/AP/2016). All the participants were informed about study details and informed consent was obtained before the initiation of study.

Inclusion criteria

i) Patients with age greater than 18 years old ii) Patients agreed to participate voluntarily with written consent form iii) Patients who were admitted as inpatients in the study duration.

Exclusion criteria

i) Patients who were hospitalized less than 48 h ii) Patients admitted to pediatrics and gynecology ward.

Study Procedure

A total of 244 patients, who met the inclusion criteria, were recruited into the study. A suitable data collection form was designed for use in the study. The sources of data were patient case sheets and laboratory data. All the recorded data was reviewed independently to identify 'triggers' and when a trigger was found, patient record was investigated in depth to determine whether an ADR occurred. If an ADR was discovered incidentally when going through the patient charts, without the presence of a specific trigger, this ADR was also considered and recorded as a "non-triggered" or "spontaneous" ADR, in accordance with the IHI methodology.

Harm categorization and causality were assessed for observed ADRs using National Coordinating Council for Medication Error Reporting and Prevention Index (NCC MERP) and Naranjo scale respectively. Positive Predictive Value (PPV) was calculated for each trigger as, number of ADRs identified with the trigger/number of triggers found in the patient charts.

Identification of Triggers

The (IHI) simplified the manual medical record review process and developed (GTT) consisting of 19 triggers to monitor adverse events rates in a way that was easy to replicate in hospitals, with or without computerized records.[7] But, in our study, modified IHI trigger tool consisting of 16 triggers was used. List of modified IHI global triggers were presented in Table 1.

Clinical Outcomes

The primary outcome was to assess incidence of ADRs using trigger tool and traditional approach. The secondary outcome was to identify the factors associated with them.

RESULTS

During the study period, a total of 244 patients were admitted into the hospital. Of which, 193 triggers were identified in 125 patients and 93 ADRs were found in 81 patients. Out of which 64 ADRs (68.81%) were found by triggers and 29 ADRs (31.18%) were found spontaneously without the presence of a trigger. Out of 81 patients with ADR's, [45 (55.56%)] were females and [36 (44.44%)] were males (Figure 1).

The frequency distribution of triggers used to identify suspected ADRs were as follows. Laboratory triggers accounted for [34 (36.55%)] followed by medication triggers contributed for [27 (29.03%)] and clinical triggers [3 (3.22%)] (Figure 1).

Table 1: List of modified IHI Global Triggers followed in the study.

T1–Abrupt Medication Stop	T2–Glucose Less than 50 mg/dl
T3–Anti-Emetic Administration	T4–Vitamin K Administration
T5–International Normalized Ratio (INR) Greater than 6	T6–Rising BUN or Serum Creatinine Two Times (2X) over Baseline
T7-Rash	T8-Antidiarrheals
T9-WBC count <3000 cells/cu.mm	T10-Elevated ALT/AST levels
T11-Hypokalemia	T12-Hyperkalemia
T13-Hyponatremia	T14-Decrease in Haemoglobin or Haematocrit of 25% or Greater
T15-Platelet Count Less than 50,000	T16-Hypotension

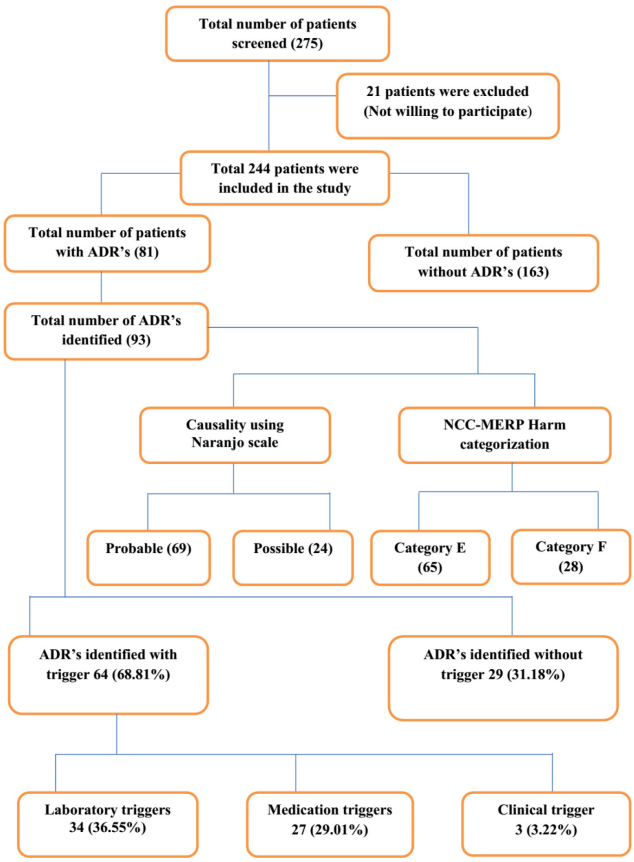

Figure 1: An illustration of study design and summarized results.

The Naranjo probability scale was applied to the study participants to determine the strength of the causal relationship with the drugs used by the patients and implicated in the occurrence of each ADR. The results of degree of causality assessment were as follows. Of 93 total ADRs, 69 (74.19%) were probable while 24 (25.81%) were possible the severity of harm of every ADR was scored using categories E to I of the National Coordinating Council for Medication Error Reporting and Prevention (NCC - MERP) severity scoring scale. The patients accounted for severity of ADRs were, 65 (69.89%) of category E, 28 (30.11%) of category F. Harm category E are more than harm category F (Figure 1).

Hypokalemia (21.50%) trigger has most frequently observed followed by the anti-emetics (13.97%), laxatives (9.67%), decreased hemoglobin (3.22%), hyponatremia (3.22%), hyperkalemia (3.22%), rash (3.22%), serum glucose <50mg/dl (2.15%), vitamin K (2.15%), INR >6 (1.07%), anti-diarrheal agents (1.07%), elevated AST/ALT levels (1.07%), platelet count <50,000 (1.07%) Positive predictive value (PPV) was found to be higher (1) for the triggers "Serum glucose <50mg/dl", "Rash" and "Platelet count <50,000". Next higher PPV of 0.67 was observed for the trigger "hypokalemia". This is followed by PPV of 0. 57 for anti-emetics trigger and INR>6, cough suppressants. The data was shown in Table 2.

The descending order of organ systems affected by ADRs was as follows. Gastrointestinal system (GI, 43.01%) > cardiovascular (29.03%) >Hematological (9.67%), Endocrine (4.30%), Respiratory (4.30%), Dermatological (3.22%) and Hepatic, Renal and Ophthalmic system (2 each, 2.15%) (Table 3).

DISCUSSION

The incidence of ADRs observed in our study period (38.1%) is remarkably higher in comparison to the incidence of other studies using different traditional methods. Our results are supported by similar previous research findings. A study conducted at a teaching hospital in Belgium by Carnevali *et al.* reported 25% incidence of ADRs.[10] Nonetheless, the incidence of ADRs in our study is lower than other study where the incidence was found to be 41%.[11]

Approximately 2/3rd (68.81%) of ADRs were detected by triggers and 1/3rd (31.18%) of ADRs were found spontaneously without the presence of a trigger. It implies that number of ADRs identified by trigger tool method is remarkably increased in comparison to the conventional method does. Our result is further supported by numerous studies reported that trigger tool method is more effective than conventional approach.[12-13]

Table 2: Positive predictive value (PPV) (effectiveness) of the triggers applied to identify adverse drug reactions (ADRs) in patient records of hospitalized patients.

Triggers	Number of positive triggers (A)	Number of ADRs (B)	PPV (B/A)
Abrupt medication stop	03	0	0
Serum glucose <50mg/dl	02	02	1
Anti emetics	23	13	0.57
Vitamin K	06	02	0.33
INR >6	02	1	0.50
Rise in Serum creatinine	03	0	0
Rash	03	03	1
Anti-diarrheal drugs	03	01	0.33
Laxatives	26	09	0.35
WBC Count <3000 cells/cu.mm	01	0	0
Elevated ALT/AST levels	05	01	0.20
Hypokalemia	30	20	0.67
Hyperkalemia	17	03	0.18
Hyponatremia	14	03	0.21
Decreased Hemoglobin (greater than 25%)	40	03	0.07
Platelet count <50,000	01	01	1
Hypotension	10	0	0
Cough Suppressants	04	02	0.50

Table 3: Frequency distribution of ADRs affecting organ system.

Organ system effected	Number of ADR's
Gastrointestinal system	40 (43.01%)
Cardiovascular system	27 (29.03%)
Hematological system	09 (9.67%)
Endocrine system	04 (4.30%)
Respiratory system	04 (4.30%)
Dermatological system	03 (3.22%)
Hepatic system	02 (2.15%)
Ophthalmological system	02 (2.15%)
Renal system	02 (2.15%)

Our study results also indicated that laboratory triggers were more contributed to detect ADRs followed by medication triggers and clinical triggers while a study conducted by Ganachari *et al.* (2013) indicated that suspected ADRs were identified majorly by medication triggers followed by laboratory trigger tools and clinical triggers.[14]

Most frequent trigger was hypokalemia (21.50%) in our study followed by anti-emetics, laxatives, rash, hyperkalemia, hyponatremia, decreased hemoglobin greater than 25%, serum glucose <50mg/dl, vitamin K (2.15%), INR >6 (1.07%), and few triggers resulted in no ADRs such as rise in serum creatinine, WBC count <3000 cells/cu.mm and hypotension. High frequent hypokalemia could probably be explained by higher utilization pattens of diuretics in cardiovascular patients of study population. However, PPV of hypokalemia was 0.67. It is the second most frequent trigger useful to identify ADRs. On the other hand, "hypoglycemia, rash and platelet count less than 50,000" were found to have highest PPV. Trigger tool approach was more efficient in identifying ADRs such as skin rash, blood sugar <50 mg/dl and platelet count <50,000. Our results were also similar to the findings by Rozenfeld *et al.* (2013) wherein triggers like skin rash and blood sugar <50mg/dl were identified in 1/3rd of adverse events.[15] On the contrary, Naessens *et al.* resulted in the maximum probability of anti-emetic (32%) trigger followed by the Diphenhydramine (10%), abrupt medication stop (8%), transfer to higher level of care (4.9%), over-sedation/ Hypotension (3.8%), Vitamin K administration (3.2%), high serum creatinine (2.6%) and glucose less than 50 mg/dl (2.2%).[16]

Causality assessment results implied that probable ADRs accounts for 74.17% while possible contributed for 25.81%. Our study showed similarity with the study by Arulmani *et al.* wherein 102 (62.2%) reactions were

assessed to be probable, 52 (31.7%) as possible and 10 (6.1%) as definite.[17] NCC MERP scale was used for assessing the severity of ADRs. Category E ADRs accounted for 69.89% while Category F contributed for 30.11% which was in concordance with the study conducted by Naessens *et al.* wherein most of ADEs falls under category E.[16] On the other hand, our study was in contrast to Rutberg *et al.* study reported that more ADEs under category F.[18] The organ system is most affected by ADRs in our study was gastrointestinal system followed by cardiovascular system. Our results were like the previous study conducted by Ganachari *et al.* wherein cardiovascular system is most affected followed by endocrine and neurological systems.[14]

CONCLUSION

Improved safety for patients is a universal priority in health care. However, efforts to impact meaningfully on safety and to reduce harm have been slowed by methodologies that fail to identify and quantify relevant clinical mishaps accurately. This study draws attention to the problem of ADRs in hospitalized patients and offers a methodological alternative by using modified IHI trigger tool. Our results suggest that trigger tool may be useful to identify ADR in hospitals twice as more efficiently when compared to traditional ADR identification methods.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

ABBREVIATIONS

IHI: Institute for Health care Improvement; **GTT:** Global Trigger Tool; **ADR:** Adverse Drug Reaction; **ADE:** Adverse Drug Event; NCC **MERP:** National Coordinating Council for Medication Error Reporting and. Prevention; **BMJ:** British Medical Journal; **PPV:** Positive Predictive Value; **CDSCO:** Central Drugs Standard Control Organization.

SUMMARY

Trigger tool approach is highly effective in the identification of ADRs in comparison to traditional approach. This method enables health care professionals including pharmacists for easy identification and reporting of ADRs. This could further increase the reporting of observed ADRs.

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