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Evaluation of Performance of IHI Global Trigger Tool in Identification of Adverse Drug Events: A Prospective Observational Study

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Authors' contributions

This work was carried out in collaboration among all authors. Author NG designed the study, performed the statistical analysis, wrote the protocol and wrote the first draft of the manuscript. Authors YKN, KP, LJ, VRG, KVV, and PB helps in hypothesis framing, literature review, design, data collection, data entry and managed the analyses of the study. All authors read and approved the final manuscript.

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ABSTRACT

Aims: The study aims to evaluate the performance of the Institute for Healthcare Improvement (IHI) global trigger tool in the identification of adverse drug events.
Study design: Prospective observational study.
Place and duration of study: The study was conducted in a General Medicine department of a

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secondary care referral hospital located in rural, resource-limited settings of Bathalapalli, Anantapur district, Andhra Pradesh, India. The study was conducted for a period of six months, from June 2019 to November 2019.

Methodology: A pre-designed data collection form was used to collect the data from the study participants. The required data was obtained from the patient case sheet, lab reports, treatment charts, daily nursing notes, daily physician notes, and direct patient interviews. The global trigger tool developed by IHI was used for the rapid review of inpatient medical records and to generate clues for the identification of ADEs. Descriptive statistics were used to represent the findings of demographics, clinical characteristics, ADE profiles, IHI triggers, and clinical alterations. ADE incidence was shown in a measure of ADE per 1000 patient days. IHI global trigger tool performance in detecting ADE was measured by sensitivity, specificity, positive predictive value, and negative predictive value.

Results: A total of 192 patients were enrolled in the study. Among them, 225 triggers and 123 ADEs were detected. The incidence of ADEs in the inpatients estimated by the IHI method was estimated as; 20.2 ADEs per 1000 patient days,64.0ADEs per 100 admissions**,** 56.2percent of admissions with ADE. Majority of ADEs are shown possible relationship with drug (60; 48.7%), level-2 severity (49; 39.8%), and not preventable (52; 42.2%). Most IHI global triggers showed high sensitivity, specificity, positive predictive value, and negative predictive value for detecting ADEs.

Conclusion: The study shows that most of the triggers in the IHI Trigger tool have shown good accuracy in identifying ADEs. Thus, using the IHI Trigger Tool to identify ADEs can help to improve patient safety. Therefore, the study recommends incorporating IHI global trigger tool in routine, conventional ADE screening techniques to improve the detection rate and promote drug safety.

Keywords: ADE, causality; IHI trigger tool; severity; sensitivity; specificity; preventability.

ABBREVIATIONS

ADE : Adverse Drug Event
AST : Aspartate Transaminase
ALT : Alanine Transaminase
IRB : Institutional Review Board
IHI : Institute for Healthcare Improvement
GCP: Good Clinical Practice
GTT : Global Trigger Tool
NPV : Negative Predictive Value
PPV : Positive Predictive Value

1. INTRODUCTION

The advancements in the drug discovery process have enabled surprising benefits for the patients; concomitantly, there was a substantial rise in the incidence of adverse drug reactions (ADRs) or adverse drug events (ADEs) [1]. ADRs are the critical cause of hospitalization, morbidity, and fatality [2]. Patients experiencing ADRs have prolonged hospital stay and shares high financial burden than those who do not develop ADRs [3]. The risk factors for ADRs are multi-factorial and include age, gender, race, genetics, polypharmacy, multiple diseases, and off-label use of drugs [4]. Globally, it was estimated that 3-7% of all hospitalizations result from ADRs, and 10-20% of inpatients suffer from drug-induced adverse reactions [5]. In India, the findings of various studies revealed that 2.9%-5.6% of all hospital admissions are due to ADEs, and 35% of the hospitalized patients experience an ADE during their hospital stay [6]. Patient safety is the primary health perspective for all policymakers and healthcare providers. Therefore, all healthcare providers need to monitor, detect, analyze, treat and prevent ADEs in hospital settings.

Different techniques like spontaneous reporting, prescription event monitoring, electronic health record mining, and record linkage are used globally to identify adverse drug events and associated risk factors in healthcare settings [7]. The major demerit for all these conventional techniques was a delay in the detection and prevention of ADEs. Researchers proposed that traditional methods are the potential to detect very few (10-20%) of ADEs, and a majority (90-95%) of these are harmless to patients [8]. Using triggers during a review of medical records is an alternative approach to overcome the problem posed by conventional methodsin detecting ADEs. The Institute for Healthcare Improvement (IHI) developed a global trigger tool (GTT) for the rapid review of inpatient medical records and to generate clues for the identification of ADEs [9]. The tool consists of triggers, like medicines underuse, laboratory results, and clinical outcomes that will act as hints to identify ADEs [10,11]. The monitoring of ADEs using 'triggers'

is a trend in healthcare services in developed countries to enhance adverse drug event detection [12–17]. Several studies performed in many countries using the IHI global trigger tool to identify ADEs [18–21].

In Indian hospital settings, the use of trigger tools in detecting ADEs was not well addressed. Therefore, the study was first time conducted in resource-limited rural hospital settings of south India, which aims to evaluate the performance of the IHI global trigger tool in the identification ADEs.

2. MATERIALS AND METHODS

2.1 Study Design and Settings

A prospective observational study was conducted over a period of six months, from June 2019 to November 2019. The study was conducted in a General Medicine department of a secondary care referral hospital located in rural, resource-limited settings of Bathalapalli, Anantapur district, Andhra Pradesh, India.

2.2 Study Criteria

Patients aged more than 18 years, irrespective of gender, taking treatment on an inpatient basis, and stay in the hospital for at least 48 hours are eligible to participate in the study. Patients who are unwilling to participate and whose medical records are incomplete in drug administration, laboratory parameters, past medical history, and discharge summary are excluded from our study.

2.3 Study Tool

The study tool comprises demographics, clinical information, IHI triggers, and clinical alterations.

2.3.1 Demographics

The patient demographic details like inpatient registration number, age, gender, date of admission, date of discharge, and audit data were included in the study tool.

2.3.2 Clinical information

The patient clinical information like chief complaints, past medical and medication history, social history, vitals, laboratory parameters, diagnosis, drug therapy, new complaints, and length of hospital stay recorded in the study tool.

2.3.3 IHI triggers

The study tool comprises IHI global medication triggers to assess ADEs. A total of 18 triggers were included in the tool. The 18 triggers included are; vitamin K administration, antihistamine use, Flumazenil use, Naloxone use, anti-emetic use, oversedation/hypotension, abrupt medication stop, laxatives, anti-diarrheal, C.difficle positive, APTT>100 seconds, INR>4, elevated AST/ALT, hypoglycemia, rise in BUN/serum creatinine, WBC<$3.0x10^9$/L, platelet count<$50x10^9$/L and reduced hemoglobin concentration.

2.3.4 Clinical alterations

Tigger-specific clinical alternations were extracted from the various published studies. A total of 18 clinical alterations were identified that match the individual trigger. The matched trigger with clinical alteration gives clues for the identification of ADE. The 18 clinical alterations included are; hemorrhage, rash/allergy, bradycardia, change in respiratory pattern, vomiting, lethargy/drowsiness/falls/hypotension, any new clinical feature, constipation, diarrhea, dysentery, bleeding, hemorrhage, hepatic lesion/jaundice, hypoglycemia, renal lesions, opportunistic infection, bleeding, and anemia.

2.4 Study Procedure

Patients who met the study criteria were enrolled in the study. A pre-designed data collection form was used to collect the data from the study participants. The required data was obtained from the patient case sheet, lab reports, treatment charts, daily nursing notes, daily physician notes, and direct patient interviews.

The data was collected by two separate teams (Team A and Team B). Each team was framed to comprise a pharmacist and a nurse trained in IHI methodology for identifying medication module triggers and their specific clinical alterations in the medical record review process. Team-A independently screens the medical records and identifies the IHI triggers present in each patient. Similarly, Team-B will be screen only for the clinical alterations among the same subjects in the study. The anonymity of the identified triggers for Team-B and clinical alterations for Team-A was maintained throughout the study to avoid bias in collecting patient information.

After data collection, the identified triggers and clinical alterations were forwarded to the concerned physician to know whether the observed triggers and clinical alterations are a part of disease progression or co-morbidity or due to drug (ADE). Once a plausible association was established between drug and ADE, the ADE data was subjected to assess causality, severity, and preventability using the Naranjo algorithm, Hartwig and Siegel and Schumock and Thornton scales.

By using the Naranjo scale, the causal association between drugs and ADEs was made as definite (≥9), probable (5-8), possible (1-4), and unlikely (0) based on the score gained. In addition, the severity of ADE was graded into mild (Level-1,2,), moderate (Level-3,4a,4b), and severe (Level-5,6,7) by using Hartwig and Siegel criteria. Finally, the preventability of ADE was divided into definitely preventable, probably preventable, and never preventableby considering Schumock and Thornton criteria.

2.5 Data Analysis

Descriptive statistics were used to represent the findings of demographics, clinical characteristics, ADE profiles, IHI triggers, and clinical alterations. ADE incidence was shown in a measure of ADE per 1000 patient days. IHI global trigger tool performance in detecting ADE was measured by sensitivity, specificity, positive predictive value, and negative predictive value. The data analysis was performed by using MedCalc statistical software. The performance measures were defined as follows;

2.5.1 Sensitivity (Se)

The proportion of days in which there was a trigger with an ADE within the total number of days in which the ADE existed.

2.5.2 Specificity (Sp)

The proportion of days in which there was no trigger within the total number of days in which the ADE did not exist.

2.5.3 Positive predictive value (PPV)

The proportion of days in which the ADE appeared within the days in which the trigger was present.

2.5.4 Negative predictive value (NPV)

The proportion of days in which there was no ADE during the days in which there was no trigger.

3. RESULTS AND DISCUSSION

A total of 192 patients were included in the study, of the majority were male (100; 52.1%), age between 18-25 years (65; 33.8%), under treatment with more than five drugs (99; 51.6%), on antibiotic therapy (151; suffering from anemia (22; 11.4%) and stayed in the hospital between 2-6 days (163; 84.8%) as shown in Table 1. The mean (± Standard deviation) age, drugs per patient, and length of hospital stay were 37.4 (±14.8), 5.6 (±2.1), and 4.9 (±2.8).

As shown in Table 2, the incidence of ADE in the inpatients estimated by the IHI method: ADE per 1000 patient days was 20.20**;** ADE per 100 admissions was 64.06**,** Percent of admissions with ADE was 56.25. Majority of ADEs are shown possible relationship with drug (60; 48.7%), level-2 severity (49; 39.8%), and not preventable (52; 42.2%) as depicted in Table 3.

Among 18 IHI triggers, elevated AST/ALT (16.8%) and antihistamine use (16.4%) are common in our study, and some triggers like Flumazenil and Naloxone use were not identified. Of 18 clinical alterations, tachycardia (23.4%) and nausea and vomiting (16.3%) are majorly observed in our study. Matching and distribution of the IHI trigger and clinical alterations were represented in Table 4.

The performance indicators like sensitivity, specificity, positive predictive value, and negative predictive value were calculated only for those triggers showing a plausible ADE association. Naloxone use, flumazenil use, INR>4, APTT >100sec, and antidiarrheal use were not identified in the review of medical records during our study. So, these triggers were not subjected to the data analysis. Clostridium difficile positive stool trigger was observed but did not have a plausible association with ADE, so it was not evaluated.

Table 1. Demographics and clinical characteristics of study subjects (n=192)

Variable	Frequency (%)
Gender	
Male	100 (52.08)
Female	92 (49.71)
Age (Mean ± SD)	37.40 ± 14.84
18-25	65 (33.85)
25-32	24 (12.5)
32-39	17 (8.85)
39-46	22 (11.45)
46-53	25 (13.02)
53-60	16 (8.33)
60-67	10 (5.20)
67-74	8 (4.16)
74-81	5 (2.60)
Drugs per patient (Mean ± SD)	5.60 ± 2.12
<3	18 (9.37)
3-5	75 (39.06)
>5	99 (51.56)
Drug category	
Anti-amoebic	7 (0.76)
Anti-asthmatics	42 (4.6)
Antibiotics	151 (16.55)
Anticoagulants and fibrinolytics	10 (1.09)
Anti-emetics	39 (4.27)
Anti-epileptics	5 (0.54)
Anthelmintic	32 (3.5)
Antihistamines	37 (4.05)
Anti-hypertensives	28 (3.07)
Antimalarials	56 (6.14)
ATT drugs	5 (0.54)
Calcium supplements	4 (0.43)
Cough suppressants and expectorants	30 (3.28)
H2- Receptor blockers	51 (5.59)
Immunosuppressants	36 (3.94)
Insulin and other oral hypoglycemic agents	10 (1.09)
Iron chelating Agents	6 (0.65)
Iron, Folic acid and Vitamin C supplements	102 (11.18)
Laxatives	13 (1.42)
NSAIDS	48 (5.26)
Opioid analgesics	17 (1.86)
Potassium chloride	8 (0.87)
Probiotics	7 (0.76)
Proton pump inhibitors	94 (10.30)
Statins	6 (0.65)
Thyroid and anti-thyroid drugs	5 (0.54)
Tricyclic antidepressants	5 (0.54)
Uricosuric agents	8 (0.87)
Vitamin B supplements	36 (3.94)
Vitamin K supplements	4 (0.43)
Others	6 (0.65)
Diagnosis	
Acute exacerbation of bronchial asthma	2 (1.02)
Acute gastroenteritis	18 (9.37)
APD with dehydration	6 (3.12)
CKI	3 (1.56)
COPD	6 (3.12)
Cellulitis	2 (1.04)
Dengue fever	9 (4.68)

Variable	Frequency (%)
Fever for evaluation	10 (5.2)
Iron + Vitamin B12 deficiency anemia	22 (11.45)
Pesticide poisoning	4 (2.08)
Pneumonia	7 (3.64)
Rickettsia fever	3 (1.56)
Snakebite	5 (2.60)
TB lymphadenitis with arthritis	3 (1.56)
Thalassemia with Iron overload	2 (1.04)
Tonsillitis	3 (1.56)
Tubercular effusion	3 (1.56)
Uncomplicated malaria	12 (6.25)
Uncontrolled DM with ketosis	14 (7.29)
URTI	13 (6.77)
UTI with DM	5 (2.60)
UTI with LRTI	17 (8.85)
UTI with enteric fever	6 (3.12)
Viral fever with post-viral arthralgia	3 (1.56)
Viral hepatitis	4 (2.08)
Others	11 (5.72)
Hospital Stay (Mean ± SD)	4.99 ± 2.80
2-6	163 (84.82)
6-10	23 (11.97)
>10	6 (3.12)

Table 2. Incidence of observed ADEs

Incidence measure	Calculation	Estimate
ADE per 1000 patient days	(Total no. of ADE/total length of stay for all records reviewed)1000	20.20
ADE per 100 admissions	(Events/total records reviewed) 100	64.06
Percent of admissions with ADE	(Records with at least one ADE/total records reviewed) 100	56.25

Table 3. ADE characteristics of the study participants (n=192)

Variable	Frequency (%)
Causality (Naranjo Algorithm)	
Definite	6 (20.3)
Probable	53 (43.0)
Possible	60 (48.7)
Unlikely	4 (3.2)
Severity (Hartwig and Siegel scale)	
Level-1	42 (34.1)
Level-2	49 (39.8)
Level-3	22 (17.8)
Level-4a	3 (2.4)
Level-4b	7 (5.6)
Level-5	0 (0)
Level-6	0 (0)
Level-7	0 (0)
Preventability (Schumock and Thornton scale)	
Definitely Preventable	25 (20.3)
Probable preventable	46 (37.3)
Not preventable	52 (42.2)

Table 4. Distribution of IHI global medication triggers and clinical alterations (ADEs)

Trigger	No. (%)	Clinical alteration	No. (%)
Vitamin K administration	4 (2.08)	Hemorrhage	1 (0.5)
Antihistamine use	37 (19.2)	Rash, allergy	5 (2.6)
Flumazenil use	0(0.0)	Bradycardia	1 (0.5)
Naloxone use	0(0.0)	Change in respiratory pattern	9 (4.68)
Anti-emetic use	30 (15.6)	Vomiting	13 (6.77)
Over sedation /hypotension	26 (13.5)	Lethargy, drowsiness, falls, hypotension	15 (13.0)
Abrupt medication stops	28 (14.5)	Any new clinical manifestation, hyperglycemia, hypertension and others	31 (5.72)
Laxatives	10 (5.2)	Constipation	5 (2.6)
Anti-diarrheal	0 (0.0)	Diarrhea	3 (1.5)
C.difficle positive	2 (1.0)	Dysentery	0 (0.0)
APTT >100 sec	0 (0.0)	Bleeding	0(0.0)
INR>4	0 (0.0)	Hemorrhage/bleeding	0(0.0)
Elevated AST/ALT levels	38 (19.7)	Hepatic lesion, jaundice	13 (6.77)
Hypoglycemia: Serum glucose <3.0 mol/L	17 (8.8)	Hypoglycemia, tachycardia	23 ()
Rise in BUN/Serum creatinine two times over baseline	5 (2.6)	Renal lesion	4 (2.0)
WBC<3.0x10^9/L	3(1.56)	Opportunistic infection	2 (1.04)
Platelet count <50x 10^9/L	20 (10.4)	Bleeding	7(3.64)
Decrease in hemoglobin or hematocrit of 25% or greater	17 (8.8)	Anemia	9 (4.68)

The highest sensitivity was observed for triggers like vitamin-K administration, anti-emetic use, over sedation/hypotension, laxatives, hypoglycemia, WBC <3x109, decreased hemoglobin, and elevated AST/ALT platelet <50x109, and abrupt medication stop. The highest specificity was observed for antihistamine use, elevated AST/ALT, anti-emetic use, platelet count <109, and laxative rising bun/serum creatinine two times over baseline. The highest positive predictive value was observed for hypoglycemia followed by elevated AST/ALT, decreased hemoglobin, elevated BUN/serum creatinine two times over baseline. The highest negative predictive value was observed for vitamin-K administration, anti-emetic use, over sedation/ hypotension, laxatives, hypoglycemia, WBC <3x109, and decreased hemoglobin followed by antihistamine use and platelet count <50x109. The findings of the performance of the IHI global trigger were represented in Table 5.

The study provides evidence on the accuracy of the IHI trigger methodology in detecting ADEs occurring in rural inpatient hospital settings of India. Among 18 triggers, we found 12 plausible associations (66.6%) between the trigger and occurred ADE. The proportion of plausible associations with triggers was high in our study compared to a public university hospital located in Brazil [22]. The findings of our research revealed that the incidence of ADEs per 1000 patient days was low (20.2) compared to the other studies conducted in China, Turkey, and Sweden [23–25]. The high rate of incidence was reported in other studies was due to the enrollment of the geriatric population for screening of ADEs. The majority of the study population belonged to 18-25 years of age, so ADEs of the severe level was not observed, and the hospital stay of a majority of the study subjects was not extended due to ADE. Most study subjects had antibiotics (16.55) in their treatment chart, followed by Iron and folic acid supplements (11.18). Most of the study subjects had >5 drugs in their medication administration chart, which may be the primary cause for observed ADEs. The majority of the observed ADE were of possible causality (48.7), mild severity (39.8), and were not preventable (42.2).

Table 5. Performance of IHI global triggers in the detection of ADEs

Triggers	Absolute frequency	Plausible association	Sensitivity (95%CI)	Specificity (95%CI)	Positive predictive Value (95%CI)	Negative predictive value (95%CI)
Vit K administration	4	1	100 (39.7 - 100.0)	77.3 (54.6 - 92.2)	44.4 (27.0-63.3)	100.00
Anti-histamine use	37	5	83.3 (35.9 - 99.6)	93.6 (87.2 - 97.4)	5.22 (1.9 -11.0)	99.0 (94.4-99.8)
Anti-emetic use	30	9	100 (66.4 - 100.0)	79.31 (70.8 - 86.3)	27.3 (20.8 - 34.9)	100
Over- sedation/ hypotension	26	15	100 (81.5 - 100.0)	50.7 (38.2 - 63.2)	35.3 (29.9 - 41.0)	100
Abrupt medication stops	28	11	90.0 (76.3 - 97.2)	73.7 (63.9 - 82.1)	58.1 (49.5 - 66.2)	94.8 (87.7 - 97.9)
Laxatives	10	5	100 (59.0 - 100.0)	78.4 (61.8 -90.2)	46.67 (32.1 - 61.8)	100
Elevated AST/ALT	38	13	98.0 (89.3 - 99.9)	83.9 (76.5 - 89.8)	70.0 (61.1 - 77.6)	99.1 (94.0 - 99.9)
Hypoglycemia: Serum glucose <3.0mol/L	17	15	100 (78.2 - 100.0)	50.0 (6.8 - 93.2)	88.24 (73.8 - 95.2)	100
WBC 3X10^9/L	3	2	100 (2.5 -100.0)	66.6 (22.3 - 95.7)	33.3 (13.9 -60.8)	100
Platelet count <50x10^9/L	20	7	93.33 (68.0 - 99.8)	79.22 (68.4 - 87.6)	46.6 (35.6 - 58.0)	98.4 (90.1 - 99.7)
Decrease in Hemoglobin or Hematocrit of 25% or Greater	17	9	100 (86.8 - 100.0)	76.8 (63.6 - 87.0)	66.7 (55.4 - 76.3)	100
Rising BUN/Serum Creatinine100% Two Times (2x) Over Baseline	5	4	52.38 (29.8 - 74.3)	77.4 (58.9 - 90.4)	61.1 (42.1 - 77.2)	70.6 (59.6 - 79.6)

Our study observed that ADEs per 100 admissions was 64.06, which was high compared to other studies conducted in Belgium (26 ADE per 100 admissions) and Turkey (29.39 ADE per 100 admissions). The high ADEs per 100 admissions observed in our study were due to fewer records reviewed (n = 192) than Turkish (n=219) and Belgian. (n=240) studies. [26,27].

The study was conducted in General Medicine Department, where Benzodiazepines, opioid analgesics, heparin were not majorly prescribed. Also, irrational antibiotic use was not observed during the study period, so the following six triggers include flumazenil use, naloxone use, Clostridium positive stool, Anti-diarrheal, APTT>100 sec, INR>4 were not identified during the study. According to our research, the modified IHI Trigger tool showed good accuracy in detecting ADEs that coincide with Turkish, Australian, and Austrian studies [24,28,29]. Our results contradict Denmark and Brazilian studies, which do not recommend using IHI GTT until additional evaluation studies on IHI GTT were conducted [30,31].

3.1 Strengths and Limitations

The strengths of our study include its prospective nature, which prevented the loss of patient-related information, which may result due to insufficient documentation of patient data by the health care professionals in the patient case sheets and omission of documentation of important information related to the patient due to lack of time or ignorance of documentation of minor problems of the patient.

The limitations of our study were that it is a single-center study and done in only a single department, i.e., the Department of medicine, some triggers were not identified, and we could not identify the ADE associated with those triggers. Therefore, we are not sure whether we have identified all the ADE that have occurred during our study period.

4. CONCLUSION

The study shows that most of the triggers in the IHI Trigger tool have shown good accuracy in identifying ADEs. Thus, using theIHI Trigger Tool to identify ADEs can help to improve patient safety. Therefore, the study recommends incorporating IHI global trigger tool in routine, conventional ADE screening techniques to improve the detection rate and promote drug safety.

DISCLAIMER

The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

CONSENT AND ETHICAL APPROVAL

The protocol, data collection form, informed consent procedure were approved (RIPER/IRB/PP/2019/003)by the Institutional Review Board (IRB) before enrolling the first participant into the trial. The study was conducted in adherence to ICH-GCP guidelines. Confidentiality and anonymity of the study data were maintained throughout the study. All participants were informed about study details and informed consent (Oral and written) procedure before initiating the study.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Khan Z, Muhammad K, Karatas Y, Bilen C, Khan FU, Khan FU. Pharmacovigilance and incidence of adverse drug reactions in hospitalized pediatric patients: A mini systematic review. Egypt Pediatric Association Gaz. 2020;68(1):24.
2. Oscanoa TJ, Lizaraso F, Carvajal A. Hospital admissions due to adverse drug

reactions in the elderly. A meta-analysis. Eur J Clin Pharmacol. 2017;73(6):759–70.
3. Patsuree A, Krska J, Jarernsiripornkul N. Experiences relating to adverse drug reactions in the community: a cross-sectional survey among patients and the general public in Thailand. Expert Opin Drug Saf. 2016;15(3):287–95.
4. Rashed AN, Wong ICK, Cranswick N, Tomlin S, Rascher W, Neubert A. Risk factors associated with adverse drug reactions in hospitalised children: international multicentre study. Eur J Clin Pharmacol. 2012;68(5):801–10.
5. Potlog Shchory M, Goldstein LH, Arcavi L, Shihmanter R, Berkovitch M, Levy A. Increasing adverse drug reaction reporting-How can we do better? PLoS One. 2020;15(8):e0235591.
6. Jain VV, Allison R, Beck SJ, Jain R, Mills PK, McCurley JW, et al. Impact of an integrated disease management program in reducing exacerbations in patients with severe asthma and COPD. Respiratory Medicine. 2014;108(12):1794–800.
7. Djamila Reis C, Etzana Veiga C. Efficacy of Trigger Tool in Identification of Suspected ADR in Secondary Hospital in Cape Verde. J Pharmacovigil. 2015;03(06):184.
8. Cahir C, Curran C, Byrne C, Walsh C, Hickey A, Williams DJ, et al. Adverse Drug reactions in an Ageing PopulaTion (ADAPT) study protocol: a cross-sectional and prospective cohort study of hospital admissions related to adverse drug reactions in older patients. BMJ Open. 2017;7(6):e017322.
9. Liu Y, Yan J, Xie Y, Bian Y. Establishment of a pediatric trigger tool based on Global Trigger Tool to identify adverse drug events of children: experience in a Chinese hospital. BMC Pediatr. 2020;20(1):454.
10. Rozich JD, Haraden CR, Resar RK. Adverse drug event trigger tool: a practical methodology for measuring medication related harm. Qual Saf Health Care. 2003;12(3):194–200.
11. Unbeck M, Lindemalm S, Nydert P, Ygge B-M, Nylén U, Berglund C, et al. Validation of triggers and development of a pediatric trigger tool to identify adverse events. BMC Health Serv Res. 2014;14(1):655.
12. Varallo FR, Dagli-Hernandez C, Pagotto C, de Nadai TR, Herdeiro MT, de Carvalho Mastroianni P. Confounding Variables and the Performance of Triggers in Detecting Unreported Adverse Drug Reactions. Clinical Therapeutics. 2017;39(4):686–96.
13. Matlow AG, Cronin CMG, Flintoft V, Nijssen-Jordan C, Fleming M, Brady-Fryer B, et al. Description of the development and validation of the Canadian Paediatric Trigger Tool. BMJ Quality and Safety. 2011;20(5):416–23.
14. Muething SE, Conway PH, Kloppenborg E, Lesko A, Schoettker PJ, Seid M, et al. Identifying causes of adverse events detected by an automated trigger tool through in-depth analysis. BMJ Quality and Safety. 2010;19(5):435–9.
15. Karpov A, Parcero C, Mok CPY, Panditha C, Yu E, Dempster L, et al. Performance of trigger tools in identifying adverse drug events in emergency department patients: a validation study: Performance of trigger tools in identifying adverse drug events. Br J Clin Pharmacol. 2016;82(4): 1048–57.
16. Franklin BD, Birch S, Schachter M, Barber N. Testing a trigger tool as a method of detecting harm from medication errors in a UK hospital: A pilot study. International Journal of Pharmacy Practice. 2010;18(5):305–11.
17. Giordani F, Rozenfeld S, Oliveira DFM de, Versa GLG da S, Terencio JS, Caldeira L de F, et al. Vigilância de eventos adversos a medicamentos em hospitais: aplicação e desempenho de rastreadores. Rev bras epidemiol. 2012;15(3):455–67.
18. Carnevali L, Krug B, Amant F, Van Pee D, Gérard V, de Béthune X, et al. Performance of the Adverse Drug Event Trigger Tool and the Global Trigger Tool for Identifying Adverse Drug Events: Experience in a Belgian Hospital. Ann Pharmacother. 2013;47(11):1414–9.
19. Härkänen M, Kervinen M, Ahonen J, Voutilainen A, Turunen H, Vehviläinen-Julkunen K. Patient-specific risk factors of adverse drug events in adult inpatients - evidence detected using the Global Trigger Tool method. J Clin Nurs. 2015;24(3–4):582–91.
20. Lau I, Kirkwood A. Measuring Adverse Drug Events on Hospital Medicine Units with the Institute for Healthcare Improvement Trigger Tool: A Chart Review. CJHP. 2014;67(6):423-8.
21. Rozenfeld S, Giordani F, Coelho S. Eventos adversos a medicamentos em hospital terciario: estudo piloto com rastreadores. Rev Saude Publica. 2013;47(6):1102–11.

22. Silva M das DG, Martins MAP, Viana L de G, Passaglia LG, de Menezes RR, Oliveira JA de Q, et al. Evaluation of accuracy of IHI Trigger Tool in identifying adverse drug events: A prospective observational study: Evaluation of accuracy of triggers. Br J Clin Pharmacol. 2018;84(10):2252–9.
23. Hu Q, Wu B, Zhan M, Jia W, Huang Y, Xu T. Adverse events identified by the global trigger tool at a university hospital: A retrospective medical record review. J Evid Based Med. 2019;12(2):91–7.
24. Kurutkan MN, Usta E, Orhan F, Simsekler MCE. Application of the IHI Global Trigger Tool in measuring the adverse event rate in a Turkish healthcare setting. Int J Risk Saf Med. 2015;27(1):11–21.
25. Rutberg H, Borgstedt Risberg M, Sjödahl R, Nordqvist P, Valter L, Nilsson L. Characterisations of adverse events detected in a university hospital: a 4-year study using the Global Trigger Tool method. BMJ Open. 2014;4(5):e004879.
26. Garrett PR, Sammer C, Nelson A, Paisley KA, Jones C, Shapiro E, et al. Developing and implementing a standardized process for global trigger tool application across a large health system. Joint Commission Journal on Quality and Patient Safety. 2013;39(7):292–7.
27. Carnevali L, Krug B, Amant F, Van Pee D, Gérard V, de Béthune X, et al. Performance of the Adverse Drug Event Trigger Tool and the Global Trigger Tool for Identifying Adverse Drug Events: Experience in a Belgian Hospital. Annals of Pharmacotherapy. 2013;47(11):1414–9.
28. Hibbert PD, Molloy CJ, Hooper TD, Wiles LK, Runciman WB, Lachman P, et al. The application of the Global Trigger Tool: a systematic review. Int J Qual Health Care. 2016;28(6):640–9.
29. Hoffmann-Völkl G, Kästenbauer T, Mück U, Zottl M, Huf W, Ettl B. [Detection of adverse events using IHI Global Trigger Tool during the adoption of a risk management system: A retrospective study over three years at a department for cardiovascular surgery in Vienna]. Z Evid Fortbild Qual Gesundhwes. 2018;131–132:38–45.
30. Mattsson TO, Knudsen JL, Lauritsen J, Brixen K, Herrstedt J. Assessment of the global trigger tool to measure, monitor and evaluate patient safety in cancer patients: Reliability concerns are raised. BMJ Qual Saf. 2013;22(7):571–9.
31. Silva M das DG, Martins MAP, Viana L de G, Passaglia LG, de Menezes RR, Oliveira JA de Q, et al. Evaluation of accuracy of IHI Trigger Tool in identifying adverse drug events: A prospective observational study. Br J Clin Pharmacol. 2018;84(10):2252–9.

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