Trigger tools for monitoring and reporting of adverse drug reactions in tuberculosis - A scientific tool for efficient reporting

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Abstract

The aim of the study was to use the trigger tools for efficiently detecting ADRs in Tuberculosis patients. The study was conducted in Nilgiris district, Tamil Nadu as a prospective open label study for a period of 8 months. While the patients of any age & gender under the DOTS therapy were included, the alcoholics, smokers and intensive care unit patents were excluded from the study. Prescriptions and or case sheets of the study patients were reviewed and the possible ADRs were detected by using a set of standardized trigger tools. 28 out of 180 patients experienced 34 ADRs. The incidence of ADRs was found high in male (n=21; 62%) than female (n=13; 38%). The organ systems mostly associated with the ADRs were gastrointestinal (32%), musculoskeletal (24%) and dermatological (18%). Respiratory, hematological, neurological and endocrine were the systems associated with less ADRs. Arthralgia (19.44%) was the highest number of ADR followed by diarrhea (11.11%) and vomiting (11.11%). WHO and, Hartwig and Seigel scales were used to find out the causality and severity of the ADRs. A total of 12 trigger tools found useful in detecting ADRs among which four were newly incorporated through this study. Thus, this study showed the efficiency of trigger tools, both existing and new ones towards detecting ADRs in tuberculosis patients.

Key words: Tuberculosis, Triggering tool, ADR, Severity, Prevalence

Introduction

Tuberculosis (TB) is the global public health priority as about 10.4 million people suffer with the disease. India is top in the list of 7 counties accounting for 64% of the 10.4 million new tuberculosis patients worldwide according to a latest report by the WHO[1] and the country also accounts for about a quarter of the global TB burden[2] and thus, worldwide India is the country with the highest burden of TB. Therefore, obviously the economic burden of TB in India is huge and is a great loss in terms of lives, money and workdays. It is estimated that about 170 million workdays are lost annually in the country due to the disease. Adverse drug reaction (ADR) is the leading cause of morbidity and mortality and increased health care cost. ADRs are contributing towards poor clinical outcome, hospitalization, prolongation of hospital stay, and enhanced economic burden. The national strategic plan (2017-2025) formulated by the Government of India needs to eliminate TB in India by 2025. The goals and visions of this plan are of a TB free India with zero deaths, disease and poverty due to TB[3].

The adverse drug reactions of anti-tubercular drugs may be mild to severe. Multidrug regimen can cause undesirable adverse drug reactions such as arthralgia, neurological disorders, gastrointestinal disorders, hepatotoxicity and allergic reactions. The frequency and nature of anti-TB induced ADRs have been the matter

of concern in many communities. One of the serious ADRs of anti-TB drugs is hepatotoxicity that is reported with high variability in different studies as this could be because of the genotype of patients e.g., rapid acetylator patients are more susceptible for isoniazid induced hepatotoxicity. ADRs are regarded as one of the major causes of nonadherence to anti-TB treatment at the same time alternative drugs may cause severe complications with few effects. The ADRs may also lead to prolonging of treatment, drug resistance, and treatment failure. The overall incidence of ADRs caused by anti-TB therapy ranges from 5.1% to 83.5%.

Towards detecting the medical error and ADRs, traditionally many systems are adopted those include but not limited to chart review, voluntary reporting by health care professionals, direct observations, and review of medical malpractice claims. However it is estimated that only 10% to 20% of errors are reported. To overcome such under-reporting there is a need for effective methods those can prioritize improvement in detection of ADRs. The use of trigger tools promotes a more focused and efficient chart review than other methods and thus may identify more adverse events[4].

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". A trigger may include Lab trigger, Medical trigger, and Clinician trigger. Such trigger tools make the chart review more efficient by identifying suspected AEs via laboratory values, text phrases or automated 'values' available in medical records, that is quicker than complete chart review and more sensitive than voluntary reporting. Therefore, the use of triggers promotes more focused chart review and thus may help to identify ADRs more efficiently.

This study is undertaken to utilize the existing trigger tools in the practice for identification of ADRs and also to develop and validate new trigger tools for effective monitoring and reporting of ADRs in tuberculosis patients[5].

Materials and methods

This is a prospective open label study undertaken at selected 7 TB centers in Nilgiris district for a period of 8 months with the purposive sampling. The patients of any age & gender under the DOTS therapy were included in to the study while the alcoholics, smokers and intensive care unit patents were excluded. The pharmacists and TB health visitors of DOTS center were involved in monitoring and detecting ADRs using the trigger tools with prior orientation and training given to them. The study was approved by the Institutional Review Board of the institution.

The prescriptions and or the case sheets were collected along with patients' data for monitoring. All such data were reviewed prospectively and checked extensively for utilization pattern of anti-tuberculosis drugs by their indication, category of drug, rationality of the drug prescription that includes: number of anti-tuberculosis drug, dose appropriateness, dosage forms, and therapy duration and total number of drugs in the prescriptions. The possible ADRs were identified by using the trigger tools.

The WHO's triggering tool list was evaluated and the triggers were selected to detect ADRs in the tuberculosis patients.

A new method originated in USA involves the use of 'Trigger Tools' which will be focused on the review of patient's record to highlight the adverse events and errors. An ADE trigger tool makes chart review more

efficient by identifying suspected AE via laboratory values, text phrases or automated 'values' available in medical records, which is more time effective than complete chart review and more sensitive than voluntary reporting. The use of triggers promotes more focused chart review and thus may help to identify ADRs. The data collected were entered into Microsoft Excel computer package for sorting, analysed with SPSS version 14. Descriptive statistics viz. frequencies, mean scores and attitudinal differences on sample characteristics were computed.

Results and discussion

A total of 238 tuberculosis patients visited the tuberculosis unit during the study period. Prevalence of tuberculosis patients in Nilgiris is given in **Table 1.**

Table No: 1 Prevalence of tuberculosis patients in nilgiris

S.no	TB center	No. Of patients	Prevalence
1	Ooty	36 (15.12%)	0.01%
2	Thuneri	29 (12.18%)	0.01%
3	Kothagiri	26 (10.92%)	0.01%
4	Neelakottai	49 (20.58%)	0.02%
5	Gudalur	53 (22.26%)	0.04%
6	Ketti	27 (11.34%)	0.01%
7	T.Horanalli	18 (7.56%)	0.01%

Out of these 238 patients, 180 were included into the study as per the set criteria. About 56 % (n=101) are male in which 62% experienced about 21 ADRs and among the 79 (44%) female patients, 38% experienced 13 ADRs. Higher incidence (21.67%) of ADRs was found in the adult age group (18-64 years) in comparison with the incidence of ADRs. In 2016, India was showing incidence of 2.79 million cases of tuberculosis and this statistic was classified by WHO. In Tamilnadu 77,100,000 of population was covered by the RNTCP members. Tamil Nadu stands 6th in the country in detection of new tuberculosis cases with 1.03 lakhs of new cases being reported in 2018. Data from January 1 to December 31, 2018 shows that in India 21.32 lakh new cases were reported by National Health Mission Tamilnadu[6]. The incidence of ADRs was maximum in adult group and minimum in geriatric group of patients is shown in **Table 2.** This is similar in the study reported by Kumarjit Sinha et al.,[7]

Table 2: Incidence Of Adverse Drug Reaction In Different Age Group

S.No	Age Group	Number of Patients Reviewed (n=180)	ADRs (n=34)	Adverse Drug Reaction Incidence percentage	Male	Female
1	<18 Pediatric	14(7.77%)	1(2.94%)	7.14%	1	0
2	19-64 Adults	143(79.44%)	31(91.17%)	21.67%	20	11
3	>65 Geriatrics	23(12.77%)	2 (5.88%)	8.69%	2	0

The incidence of ADRs was maximum in adult group and minimum in geriatric group of patients is shown in Table 2.

Out of the 28 patients experienced ADRs, 19 (68%) were diagnosed with pulmonary TB and the rest (n=9; 32%) were extra pulmonary tuberculosis patients. It is also found that 11(39%) urban and 17(61%) rural experienced ADRs.

The organ systems mostly associated with ADRs were gastrointestinal (32.35%) followed by musculoskeletal (23.52%) and dermatological (17.64%) respectively. Respiratory 3%, hematological 2%) neurological 3% and endocrine systems 1% showed comparatively less ADRs.is shown in **Fig 1**

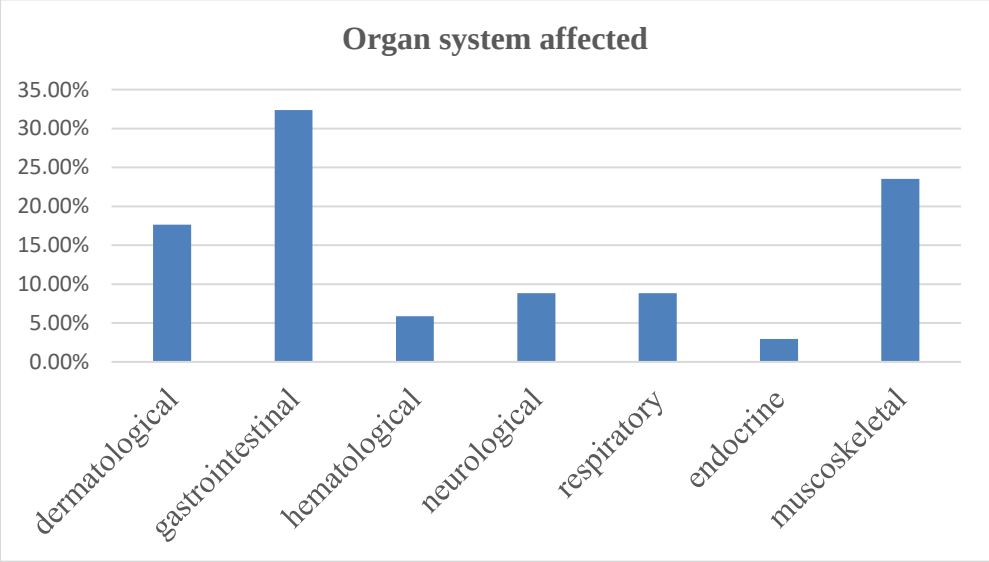

Figure 1: Incidence among different affected Organ System

In comparison with other studies, Arif I dela et al., and K V Ramnath and Ramesh studies showed that majority of ADRs were seen in gastrointestinal tract (24.5%) followed by weakness (21.23%), psychological (14.38%),

joint pain (14.38%), and respiratory (7.8%)[8,9]. Another study by Javedh Shareef et al., also showed that most common system associated with ADR was gastrointestinal system (45.5%)[10].

Severity of the ADRs was assessed by using modified Hartwig and Siegel severity assessment scale as shown in **Table 3.**

Table 3: Adverse drug reactions comparison with different level of severity by modified hartwig and siegel severity assessment scale

S.No	Severity	Levels	Adverse Drug Reaction (n=34)	Adverse Drug Reaction incidence Percentage(%)	Levels Percentage
1	Mild	Level 1 (9) Level 2 (14)	23	67.64	26.47% 41.17%
2	Moderate	Level 3 (6) Level 4(a) (1)	7	20.58	17.64% 2.94%
3	Severe	Level 5 (3) Level 7 (1)	4	11.76	8.82% 2.94%

maximum number of ADRs were under the category of mild (68%) , moderate 21% and severe 12% that is similar to the study reported by K V Ramnath and Ramesh (2012).,[8] that showed 64% ADRs were mild and 36% were moderate[9]. Another study by Javedh Shareef et al., (2018) study showed that 60.7% of the adverse drug reactions were 'moderate' and 36.4% were 'mild'[10].

As the result of ADRs the treating physicians withdrawn the drug in 14 % of the cases, altered the dose in about 3 % and in the remaining cases (83%) no changes in medication were done. Out of the 28 patients experienced ADRs were recovered in 24 (85.71%) and were unknown in 4 (14.29%) due to loss of follow up or death.

Fig 2 represents the causality assessment by the WHO scale. Accordingly, the highest ADRs fall in the category of certain (41.17%), followed by probable (23.52%) and possible (35.29%).

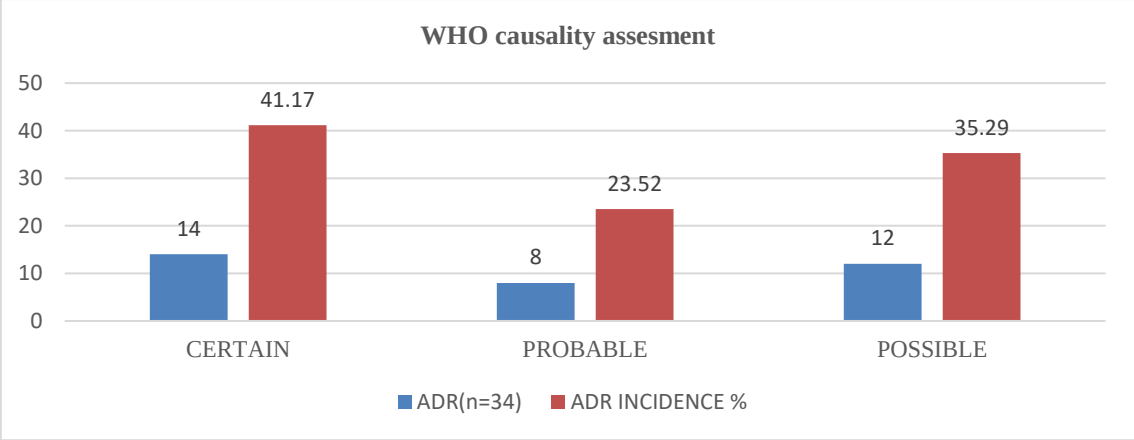

Figure 2 WHO causality assessment

This data is contradictory to the results of arif I dela et al., (2017)[8] who reported 4.79% were certain, 13.69% were probable, and 81.95% ADRs were possible category. Another study reported by K. Venkateswarlu et al., (2017) is similar to the results of this study in which majority of ADRs were found to be certain 52(65%), followed by probable 7 (28.7%), Possible 1(1.2%)[11]. Based on the suspected ADRs, five (15%) were treated with specific treatment, one condition (3%) was treated symptomatically and the remaining 28 conditions (82%) were not treated.

This study showed maximum ADRs as arthralgia (19.44%) followed by diarrhea (11.86%), vomiting (11.86%) and allergy (11.11%) and the same are listed in **Table 4.**

Table 4: Details Of The Adr And Patients

S.NO	ADR	Triggering tool	ADR (n=34)	ADR incidence percentage(%)
1	Rash	Rash	3	8.82
2	Diarrhea	Anti diarrheal	4	11.76
3	Vomiting	Anti emetic	4	11.76
4	Seizure	Seizure	1	2.94
5	Gout	Joint pain	1	2.94
6	Respiratory failure	Abrupt cessation of medication	3	8.82
7	Artharlgia	Joint pain	7	20.58
8	Gastritis	Antacid	2	5.88
9	Psychosis	Psychiatric opinion	2	5.88
10	Constipation	Laxative	1	2.94
11	Anemic	Anti anemic	2	5.88

12	Allergy	Anti allergy	2	5.88
13	Weight gain	Abnormal thyroid level	1	2.94
14	SJS	Rash	1	2.94

These results are different from the results reported by Naessens et al., (2010)[12] showed the results in maximum probability was in Anti- emetic (32%), Diphenhydramine (10%) and abrupt medication stop (8%). the study done by Takata et al., (2008)[13]; diphenhydramin (8.44), anti-emetic (1.55), Laxative (2.82), serum creatinine (3.85), Abrupt medication stop(19.7), glucose less than 50 mg/dl (0.6), over sedation/fall/lethargy/hypotension(14.9) and PTT>100s (16.7).

13 trigger tools were identified in 28 subjects. Out of which, 10 positive trigger tools were utilized to report 32(88.88%) ADRs and the triggers (like Diphenhydramine, anti emetic, anti diarrheal, antianemia, uric acd elevation, thyroid level increases and laxative). During the study new trigger are developed like antacid, psychiatric opinion, thyroid level elevation and anti anemia. Proposed triggering tool list with probable drug is shown in **Table 5.**

Table 5: Proposed triggering tool list with probable drug

S.no	ADR	Triggering tool	Probable drug	Number of patients
1	Gastritis	Abdominal pain	Rifampicin	2
2	Psychosis	Psychiatric opinion	Cyclosporine, isoniazid	2
3	Anemia	Blood test	Isoniazid	2
4	Weight gain	Thyroid level	Pyrazinamide	1

The percentage of contribution by the trigger tool in identification and reporting of suspected ADRs Medication trigger (88.88%) and laboratory trigger (11.11%). Handler et al.,stated that laboratory/ medication signal contribute 75% of preventable adrs in comparison our study resulted.

Conclusion

As ADRs are very common in tuberculosis, healthcare providers including pharmacist shall play a lead role in preventing the complication of ADRs using the trigger tools to ensure the patients safety. Thus, there is a need of training regarding the trigger tools for the healthcare providers about monitoring trigger tools for the better patient safety. In this study, such training and sensitization resulted in ADR reporting using the trigger tools in tuberculosis patients.

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Conflicts of interest

The authors do not have any Conflict of Interest.

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