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Abstract- This study describes the occurrences of adverse drug reactions (ADRs) caused by anti tubercular (TB) drugs employed in Directly Observed Treatment Short Course (DOTS) from ten years of ADR data (from 2002 to 2012) reported in various articles. The frequency of each type of ADR was analyzed and compared. A total of 10,219 patients were studied. Among them, 8,047 (78.75%) patients demonstrated positive responses to at least one type of ADR. Dermatological reactions predominated among the ADRs which occurred in 4389 (42.95%) patients followed by hepatotoxicity in 1634 (15.99%) cases. Female patients were more prone to ADRs as compared to the male patients. The occurrence of ADRs is mainly attributed to the combination therapy along with the prolonged medication period. A colossal amount of ADRs were observed during the study which must be monitored and managed properly throughout the DOTS therapy in order to prevent life-threatening harmful effects.

Keywords: tuberculosis, adverse drug reactions, dots.

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Comparative Analysis of Adverse drug Reactions in Directly Observed Treatment Short Course (DOTS) in TB Patients

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Abstract- This study describes the occurrences of adverse drug reactions (ADRs) caused by anti tubercular (TB) drugs employed in Directly Observed Treatment Short Course (DOTS) from ten years of ADR data (from 2002 to 2012) reported in various articles. The frequency of each type of ADR was analyzed and compared. A total of 10,219 patients were studied. Among them, 8,047 (78.75%) patients demonstrated positive responses to at least one type of ADR. Dermatological reactions predominated among the ADRs which occurred in 4389 (42.95%) patients followed by hepatotoxicity in 1634 (15.99%) cases. Female patients were more prone to ADRs as compared to the male patients. The occurrence of ADRs is mainly attributed to the combination therapy along with the prolonged medication period. A colossal amount of ADRs were observed during the study which must be monitored and managed properly throughout the DOTS therapy in order to prevent life-threatening harmful effects.

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I. INTRODUCTION

Geographically, the burden of TB is highest in Asia and Africa. India and China together account for almost 40% of the world's TB cases (WHO, 2012). TB is a highly infectious disease caused by Mycobacterium tuberculosis, which is the second leading cause of death due to infection in the world. TB is a major public health problem in Bangladesh. The country ranks 6th on the list of 22 highest burden TB countries in the world. Each hour eight persons die of the disease for which very effective treatment, free of cost, is available in Bangladesh. Before 1993 TB control was limited to TB clinics and TB hospitals. Field implementation of TB control integrated into the general health services, delivered by Upazila Health Complexes (UHC's), started back in 80s. However, National TB Control Programme (NTP) Bangladesh revised its strategies and adopted DOTS in 1993. NGO's have been involved since 1994 (NTP).

The overall goal of the NTP is to reduce morbidity, mortality and transmission of TB until the disease is no longer a public health problem. The objectives are to

detect 70% of new smear-positive pulmonary TB cases and cure at least 85 % of them by the year 2005 and be maintained thereafter to reach the Millennium Development Goal (MDG) by 2015 (NTP).

As the treatment of TB almost always involves combinations of drugs that are to be taken for a prolonged period of time, the occurrence of ADR is quite likely. Moreover, the adverse effect of one drug may be enhanced by the associated drug used which is one of the major reasons for the faulty patient treatment.

The common ADRs observed in DOTS involved mild gastritis, central nervous system, peripheral nervous system, psychiatric, dermatologic, musculoskeletal, renal, otologic, and ocular complications along with hypothyroidism, hepatitis, icterus, fever, and breathlessness (J. J. Furin et al., 2001; K. D. Tripathi, 2008; Rang & Dale, 2007).

Thus, a comprehensive understanding of the various ADRs along with their management is mandatory for the prevision, detection, and effectual TB management. It has become quite imperative to monitor the ADRs of patients on DOTS through the monitoring of ADRs and hence, the current study was undertaken.

II. MATERIALS AND METHOS

Ten years ADR data (from 2002 to 2012) in the DOTS therapy caused by anti-TB drugs previously reported in various articles were searched from referred sources and observed carefully. The observed cases of different regions are listed in Table 1.

III. RESULTS AND DISCUSSION

A total of 10219 patients were observed from previously studied articles. Among them 8047 (78.75%) patients showed at least one type of ADR. Dermatological ADRs were predominant (42.95%) which was followed by hepatotoxic reactions (15.99%). Different types of ADRs and there prevalence occurrence is depicted in Table 2 and Figure1.

The study says that, Isoniazid, rifampicin, and ethambutol are the drugs responsible for the skin reactions (F. Kurniawati et al., 2012). Arthralgia or gout which is prevalent in adults is mainly caused by isoniazid, ethambutol, and pyrazinamide that can be managed by Nonsteroidal Anti- inflammatory Drugs

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(NSAIDs). Children are less prone to hepatitis as compared to adults, mainly shown by pyrazinamide alone, isoniazid and rifampicin, isoniazid alone, and rifampicin alone. It can be reduced by starting therapy with ethambutol and pyrazinamide (F. Kurniawati et al., 2012).

The occurrence of ADRs among the female patients was marginally higher as compared to the male patients. This phenomenon is attributed to the alteration of drug responses mainly due to their lower body weight compared to the males. Different phases of life such as, pregnancy, menstruation cycles etc. also contribute to some extent in this regard (J J Furin et al., 2001; D.K.Tak et al., 2009).

ADR management should involve proper monitoring of the adverse reactions, postponing medication regimens, continuing the medication again without change and finally changing patient's treatment regimens. To reduce GI disorders antiemetic drugs and to alleviate dermatological reactions antihistamines can be administered as add on therapies.

IV. CONCLUSION

The occurrence of ADRs in the patients with DOTS is highly alarming; and immediate measures should be taken for the prevention of this phenomenon in order to minimize the potential serious health hazards including death. Pharmacists can play a significant role in the management of ADRs through patient counseling and improving their awareness.

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Table 1 : Number of Patients Observed of Different Regions (F. Kurniawati et al., 2012; Begum L. Nahar et al., 2006; A. K. Chhetri et al., 2008; K. Gholami et al., 2006; PV Kishore et al., 2008; J. I. Jeong et al., 2009; Pillai, 2008).

	Region	Country	No. of Patients
1	Sylhet Chest Disease Hospital and Sylhet Shaheed Shamsuddin Ahmed Hospital	Bangladesh	64
2	New Delhi	India	185
3	Department at Imam tertiary teaching hospital	Iran	83
4	Gangneung	Korea	57
5	Penag	Malaysia	653
6	Manipal Teaching Hospital, Pokhara	Nepal	326
7	Pokhara	Nepal	137
8	Thailand	Thailand.	8,714
Total			10,219

Table 2 : Different Types of ADRs Observed (F. Kurniawati et al., 2012; Begum L. Nahar et al., 2006; A. K. Chhetri et al., 2008; K. Gholami et al., 2006; PV Kishore et al., 2008; J. I. Jeong et al., 2009; Pillai, 2008).

Si. No.	Different ADRs	No. of Patients	Percentage
	Total no. of patients observed	10,219	100.00
1	Dermatological	4,389	42.95
2	Hepatitis	1,634	15.99
3	GI disturbance	1,004	9.82
4	Musculoskeletal	166	1.62
5	Central nervous system	86	0.84
6	Headache	37	0.36
7	Ocular	29	0.28
8	Fever	13	0.13
9	Otological	9	0.09
10	Peripheral nervous system	7	0.07
11	Renal	7	0.07
12	Breathlessness	4	0.04
13	Psychiatric	3	0.03
14	Miscellaneous	659	6.45
Total no. of ADRs observed		8,047	78.75

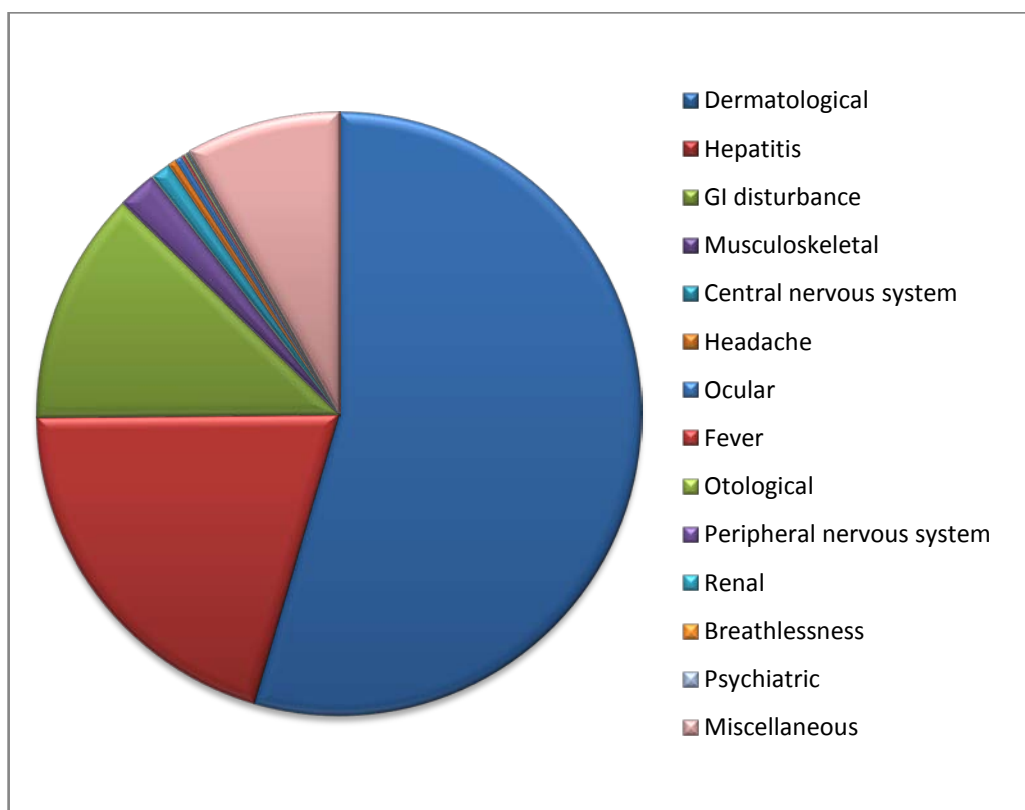


Figure 1: ADR percentages in DOTS