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Management of Adverse Effects of Drugs used to Treat Multi Drug Resistant Tuberculosis in Bangladesh: An Observational Study

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Abstract **Original Research Article**

Background & Objectives: During treatment of Multi Drug Resistance Tuberculosis, patients suffer from many adverse effects. For management of adverse effects, ancillary medications are suggested. Severe adverse effect may lead to refusal and discontinuation of treatment. Poor management of adverse effects increases the risk of default or irregular or short duration adherence to treatment and results in permanent morbidity or death. Though national TB control programmes are generally well structured, they do not collect information on adverse effects and their management directly. In this regard, pharmacovigilance should be an integral component for TB control programme. So this study had been designed to observe the clinical management of adverse effects of MDR-TB drugs in Bangladesh with objective to provide information for subjects, health workers, doctors, people and organizations concerned with the activities for prevention, control and management of MDR-TB. ***Methods:*** This observational and descriptive type of longitudinal study was carried out at the in-patient department of the National Institute for Diseases of the Chest & Hospital, Dhaka, Bangladesh. The total number of subjects included was 64.The data collection was carried out with pretested questionnaire. After the interview at the initial stage, the respondents had to take part in interview again at one month interval up to the end of 3rd month of treatment. The collected data was analyzed in terms of descriptive method. ***Results:*** The mean age of respondents was 34.76 ± 12.98 years. 20-60 years age group comprised of 80% respondents. Male to female ratio was 2:1. Regarding the adverse effects of MDR-TB drugs, 80% respondents suffered from arthalgia, 59% from anorexia, 52% from dizziness, 44% each from nausea/ vomiting and sleep disturbances. 19% each developed gastritis, hypothyroidism &psychological disorders. 17% developed impaired hearing. Peripheral neuropathy developed in 28% respondents. Serum creatinine level was raised in 03% respondents. Hypokalaemia had developed in 06% respondents. For management of adverse effects both Pyridoxine and Omeprazole had been used in 100% (64/64) cases. Among NSAIDs, in 60% (32/53) cases Paracetamol, in 17% (09/53) cases Diclofenac, in 13% (07/53) cases Etoricoxib had been used. As antiemetic, Domperidon and Ondansetron had been used in 87% and 13% cases respectively. As anxiolytic Clonazepam had been used in 85% cases. Adverse effects had been attempted to be managed at NIDCH (National Institute for Diseases of the Chest & Hospital, Mohakhali, and Dhaka) in 100% (64/64) cases. 17% (10/64) had been referred to SAHIC (Society for Assistance to Hearing Impaired Children, Mohakhali, Dhaka) and 02% (01/64) each to NIKDU (National Institute for Kidney Diseases & Urology, Sher-e- Bangla Nagar, Dhaka) and NIMH (National Institute of Mental Health, Sher-e-Bangla Nagar, Dhaka). Impaired hearing developed in 17% (11/64) respondents and among them 91% (10/11) had been sent to ENT specialist of SAHIC. Uninterrupted treatment had been continued in 86%cases. Drug dose had to be reduced in 11% cases and drug had to be stopped in 03% cases. ***Conclusion:*** The findings of this study may provide baseline information on management of adverse effects of MDR-TB drugs in Bangladesh. The information may help minimizing the treatment interruption and thus prevent propagation and dissemination of MDR-TB.

Keyword: MDR-TB, Pharmacovigilance, Bangladesh, Adverse Effect of drug.

INTRODUCTION

Tuberculosis is a major public health problem in Bangladesh. 22 countries of the world are referred to by World Health Organization as high TB burden countries. Bangladesh is one of them and fifth in position among the top five high burden countries [1].

In 1993, World Health Organization declared TB as global emergency. Nearly one third of global population is infected with *Mycobacterium tuberculosis* [2]. In spite of strong TB control programme, under close supervision of Government & World Health Organization, Bangladesh fails to escape from the claw of MDR-TB, TB caused by the strains of *Mycobacterium tuberculosis* resistant to the effects of Isoniazid and Rifampicin with or without resistance to any other drug [3].

Though the causes are microbial, clinical & programmatic, MDR-TB is essentially a man-made phenomenon [4]. Drug resistance results from improper use of antibiotics in treatment of drug susceptible TB. This 'improper use' includes administration of improper treatment regimen and failure to ensure the completion of the whole course of treatment [5].

In 2008, WHO ranked Bangladesh as 9th among 25 high priority MDR-TB countries [6]. In Bangladesh, the proportion of new TB cases with MDR-TB is 1.4% and retreatment TB cases with MDR-TB are 28.5% which indicates that the occurrence of total MDR-TB is about 4000 each year which was 3000 approximately in 2007[7, 3].

To achieve Millennium Development Goal, Bangladesh is addressing not only TB but also MDR-TB. The National Tuberculosis Control Programme of Bangladesh (NTP) has launched a programme in 2008 to treat MDR-TB.

According to National Guidelines and Operational Manual for Programmatic Management of Drug Resistant TB (2013) in Bangladesh, MDR-TB treatment regimen consists of two phases: Intensive phase and Continuation phase. Duration of intensive phase is at least 8 months provided 4 months past culture conversion and continuation phase is at least 12 months. The total treatment duration is 20 - 22 months [5].

Five anti - TB drugs are used in intensive phase: Pyrazinamide + Kanamycin + Ofloxacin + Ethionamide + Cycloserine. The drug dosages are determined by body weight of the patient. Among the drugs, Kanamycin is the only injectable one. In continuation phase Kanamycin is no longer used [4].

In Bangladesh, in both phases, drugs are administered under strict 'DOT' (Directly Observed Treatment) either in a hospitalized state at National Institute for Diseases of the Chest & Hospital, Mohakhali, Dhaka, a tertiary level hospital and research institute for the chest diseases including Pulmonary TB and the central point of treatment of drug resistant TB, or at community level where 'DOTS' (Directly Observed Treatment Short course) is provided[6, 8].

In MDR-TB, due to treatment with more toxic drugs, patients suffer from many adverse effects [9]. The common possible adverse effects produced by the drugs used to treat MDR-TB include anorexia, nausea/vomiting, diarrhoea, gastritis, allergic reaction, skin rash, hepatitis, peripheral neuropathy, hearing & visual disturbances, nephrotoxicity, hypothyroidism, psychological disorders like psychosis, depression, anxiety, suicidal ideation, seizures, arthalgia, electrolyte imbalance, dizziness, vertigo, tinnitus, headache, sleep disturbance etc. [3-5].

For management of these adverse effects, ancillary medications are suggested and these are the supporting drugs for symptomatic treatment. These ancillary drugs may eliminate or lessen the event of adverse effects and treatment of MDR- TB may be continued [4, 5]. But severe adverse effect may lead to refusal & discontinuation of treatment before smear conversion.

The management of patients with MDR-TB is yet inadequate [5]. Poor management of adverse effects increases the risk of default or irregular or short duration adherence to treatment and results in permanent morbidity or death. Again short duration chemotherapy for patients infected with drug resistant strains may create even more resistance to the drug in use which is termed as 'amplifier effect' of short course chemo therapy [3]. There may be occurrence of concomitant transmission of resistant strains of *Mycobacterium tuberculosis* to the community as well. Ongoing transmission of established MDR-TB strains in population may also further contribute to new primary drug resistant cases [5].This may lead to a burden to our economy as patients of MDR-TB are treated for a long period with less potent, more toxic & much more expensive drugs.

Though national TB programmes are generally well structured, they do not collect information on adverse effects and their management directly [10]. In Bangladesh adverse effects of drugs used in MDR-TB along with management is scantly reflected in published information on subject. In this regard, pharmacovigilance needs to be an integral component for TB control programme in Bangladesh [10].

So this study had been designed to observe the management of adverse effects of MDR-TB drugs in Bangladesh with an objective to provide information for subjects, health workers, doctors, people and

organizations concerned with the activities for prevention, control and management of MDR-TB.

MATERIALS & METHODS

This observational and descriptive type of longitudinal study had been carried out at the in-patient department of the National Institute for Diseases of the Chest & Hospital (NIDCH), Dhaka, Bangladesh. MDR-TB patients from all over the country, mostly referred cases, attend this health care facility. Thus the patients visiting this hospital provide the reflection of MDR-TB situation in Bangladesh.

The duration of the study was one year extending from July 2013 to June 2014.The study population comprised of all the patients of MDR-TB admitted in NIDCH from December 2013 to February 2014 which was a total of 110 where there were 32, 32, 46 patients in December, January and February respectively. Purposive sampling had been done to fill up the target respondents. Diagnosed and registered MDR-TB patients with a DOTs identification number who were admitted and had to stay at least three months in NIDCH were included in the study. The total number of subjects included in the study regarding inclusion and exclusion criteria was 64.

The data collection had been carried out with a predesigned pretested questionnaire containing both open and closed ended questions. Data was collected through face to face interview and data regarding supporting physical and laboratory findings were obtained from DR-TB treatment card, physical examination and laboratory reports of the respondents after taking informed written consent. After the interview at the initial stage of treatment, the respondents had to take part in interview again at one month interval up to the end of 3rd month of treatment.

The data includes information regarding the identification of respondents, their socio demographic background, co-morbidity, smoking habit, site of TB, treatment protocol, history of contact with TB or MDR-TB patients, previous history of TB treatment along with adverse effects of first line anti-TB drugs, adverse effects in MDR-TB treatment, supporting physical & laboratory findings, place of management of adverse effects and the ancillary drugs used to manage those effects.

Checking regarding weight, anemia, jaundice, vision, hearing, mental status and peripheral numbness was done at base line and at one month interval up to the end of 3rd month of treatment. Also the data containing information about laboratory findings of Hemoglobin level, cell count, serum bilirubin, ALT, serum creatinine, RBS, serum potassium was collected at base line and then monthly up to the end of 3rd month of treatment. Data about TSH was recorded at base line and at second month.

The quality of data was ensured at field level. After scrutiny, the completed questionnaire was reviewed to ensure the completeness and consistency of the collected data. The collected data was classified. The edited data had been entered into computer through Excel programme. Then the data was analyzed in terms of descriptive method which includes percentage, frequencies, means with standard deviation of findings.

The study was approved by the Ethical Review Committee of Dhaka Medical College, Dhaka, Bangladesh. Permission for data collection was obtained from the authority of NIDCH, Dhaka, Bangladesh. Informed written consent was taken from all participants before the interview.

RESULTS

A total of 64 respondents participated in the study. The study revealed that the mean age of respondents was 34.76 ± 12.98 years. 16% respondents were below the age of 20years. 05% were above the age of 60 years and the rest (44%+36%) 80% (51/64) were between 20 to 60 years.

Among the respondents, 66% were male and 34% were female with a male to female ratio of 2:1. 59% (38/64) respondents had been living in urban area and 41% (26/64) in rural area. 25% (16/64) respondents were illiterate. 20% (13/64) studied below class VI and 38% (24/64) studied below SSC. 3% (02/64) had Graduation or above degree. 52% respondents were smoker and all of them were male.

09% (06/64) were farmers and students as well. 19% (12/64) were house wives. Among the service holders 47% (08/17) were garments worker. 12% (02/17) had history of working abroad also. Most of them, 43% (20/46), had monthly income of 5000-10000/- taka. Mean income was found as10, 859/- taka per month. 55% (12/22) and 27% (06/22) female were married and unmarried respectively. Again 64% (27/42) & 36% (15/42) male were married and unmarried respectively. 09% (02/22) female were separated and widow as well but no male belonged to these groups.

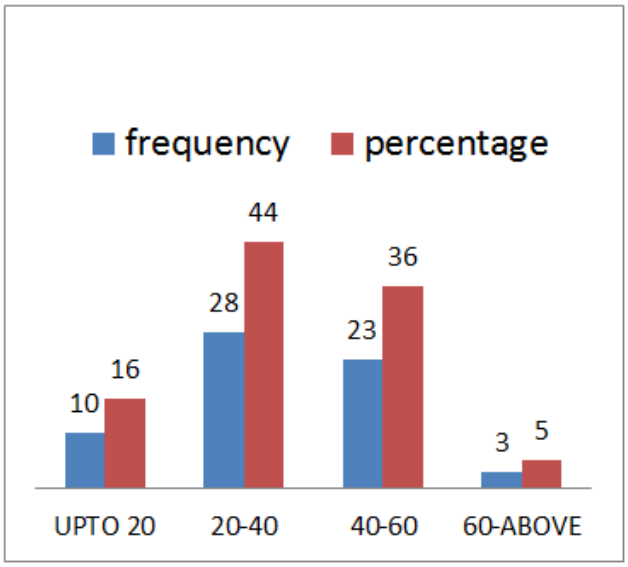

Fig-1: Distribution of respondents by Age (n =64)

72% respondents were free from co-morbidities. 14% (09/64) had been suffering from DM, 06% (04/64) from Br. Asthma, 03% (02/64) from COPD. 98% respondents had been suffering from pulmonary TB and rest 2% from extra pulmonary TB. There had been presence of TB patients in family among 17% respondents. Among the respondents, 25% were susceptible to TB (had H/O contact with TB patient), 11% were susceptible to MDR-TB (had H/O contact with MDR-TB patient) and 03% were susceptible to both TB & MDR-TB. 39% susceptible respondents had H/O contact with siblings, next 26% with father, 22% with others but none had H/O contact with spouses having TB or MDR-TB.

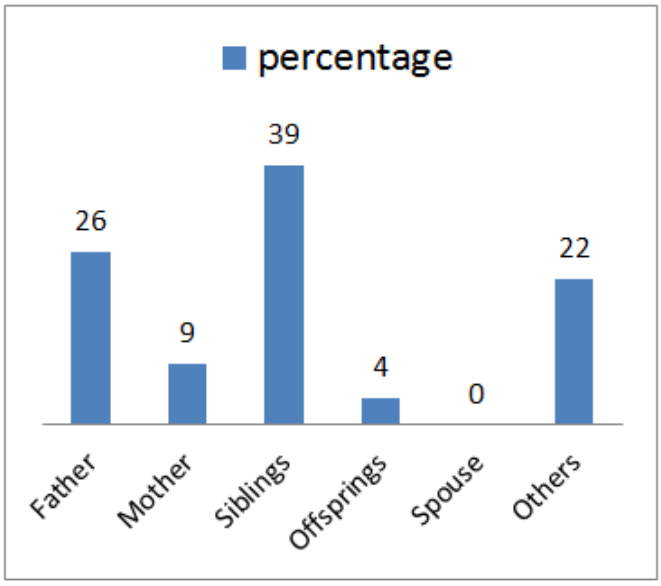

Fig-2: Distribution of Respondents by relation with Contact of TB & MDR-TB patient

69% respondents had been informed about adverse effects of 1st line Anti-TB drugs. Adverse effects had occurred in 27% respondents and rest73%was free from any adverse effects of 1st line Anti-TB drugs.

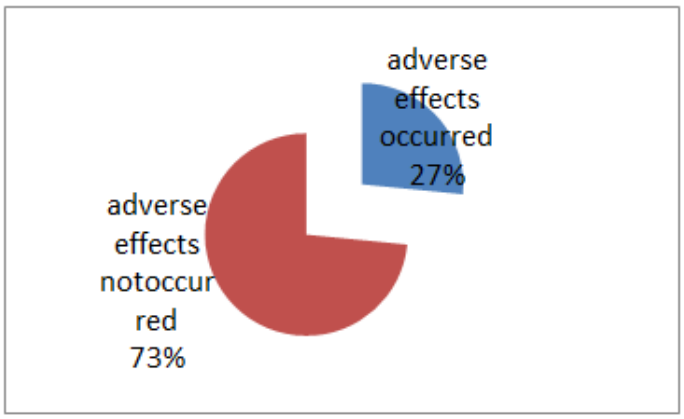

Fig-3: Distribution of Respondents by History of Adverse Effects of 1st line Anti-TB drugs (n=64)

During treatment with 1st line Anti-TB drugs 94% had been suffering from vomiting and 88% from arthalgia. 18% and 12% had been suffering from tinnitus and allergic reaction respectively. From jaundice, impaired vision, hearing loss and peripheral neuropathy there had been suffering 6% each respondents. 03% of respondents had to discontinue TB treatment due to adverse effects of 1st line Anti-TB drugs. The discontinuation of TB treatment was only temporary with duration of 7-14 days.

28% (18/64) respondents belonged to relapse of cat-l. 19% (12/64) and 14% (09/64) belonged to treatment failure respectively of cat-l & cat-ll. Again 8% (05/64) and 6% (04/64) were delayed converter of cat-l & cat-ll respectively.17% (11/64) was from relapse cat-ll and 5% (3/64) from default cat-l. 3% (02/64) were the case of primary MDR-TB.

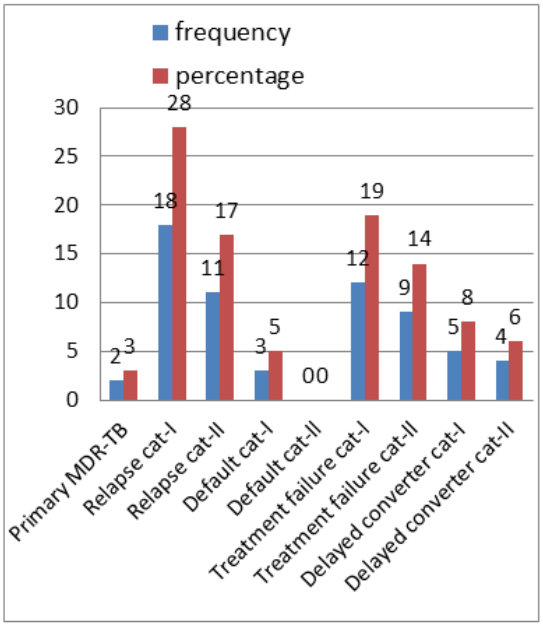

Fig-4: Distribution of respondents by Case Definition of MDR-TB (n =64)

In first three months of MDR-TB treatment, in female, mean body weight was between 39.77 and 40.86 kg and in male it was between 45.61 and 47.66 kg. Average weight gain was 01 kg and 02 kg in case of female and male respectively.

Table-1: Mean body weight of the respondents in 1st three months of treatment

Variable	Month	Female	Male
Body weight	0	39.77±4.61	45.61±6.8
Mean ± SD (kg)	1	39.81±4.43	46.45±6.8
	2	40.18±4.4	47.02±6.95
	3	40.86±4.6	47.66±9.3

Regarding the adverse effects of MDR-TB drugs, 80% (51/64) respondents suffered from arthalgia, 59% (38/64) from anorexia, 52% (33/64) from dizziness, 44% (28/64) each from nausea/vomiting and sleep disturbances. 19% (12/64) each developed gastritis, hypothyroidism & psychological disorders. In case of psychological disorders 67% (08/12) suffered from depression, 25% (03/12) from anxiety and 08% (01/12) from psychosis.

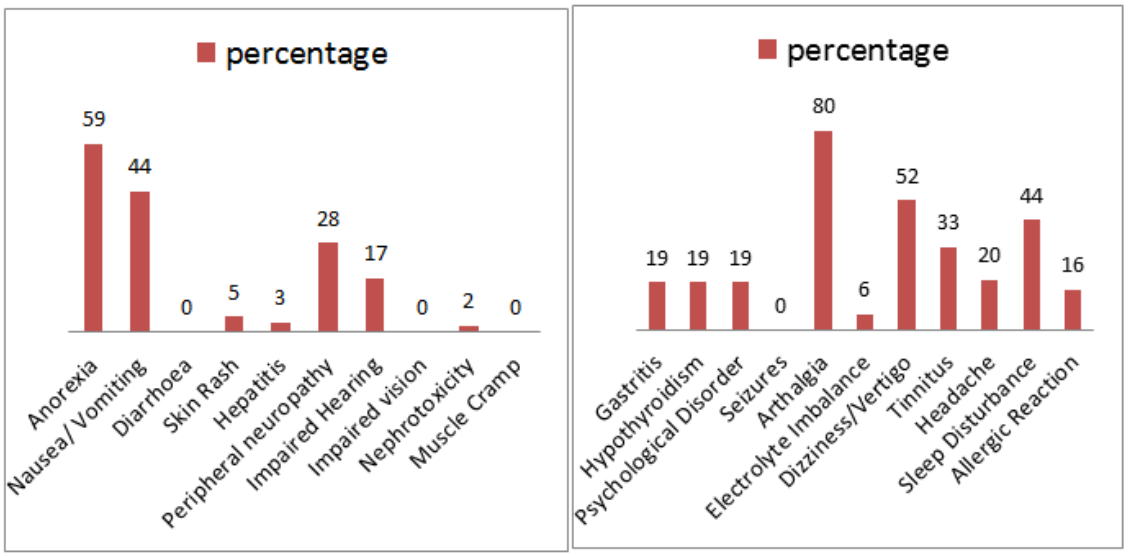

Fig-5: Distribution of Respondents by Adverse Effects of MDR- TB drugs (n=64)

17% (11/64) developed impaired hearing as well as 33% (21/66) developed tinnitus. During the treatment of MDR-TB, there aroused jaundice in two patients, in 2nd month in one patient and in 3rd month in another patient. Peripheral neuropathy developed in 28% (18/64) respondents. Among the respondents with peripheral neuropathy, 50% (09/18) were diabetic. 81% (52/64) respondents were non diabetic by Random Blood Sugar. 14% (09/64) had co-morbidity with DM and 05% (03/64) developed impaired glucose tolerance. Serum creatinine level was raised in 03% (02/64) respondents during their treatment. Serum TSH level was raised in 19% (12/64) respondents. Hypokalaemia had developed in 06% respondents.

23% (15/64) respondents had to suffer from 04 adverse effects, 16% (10/64) from 03 adverse effects, 14% (09/64) each from 05 & 06 adverse effects and 02% (01/64) from highest 11 adverse effects. Mean no. of adverse effects that the respondents had to suffer from was 05 (range 01 -11).

For management of adverse effects of MDR-TB drugs both Pyridoxine and Omeprazole had been used in 100% (64/64) cases. Clonazepam had been used in 63% (40/64) cases and Paracetamol in 50% (32/64) cases.

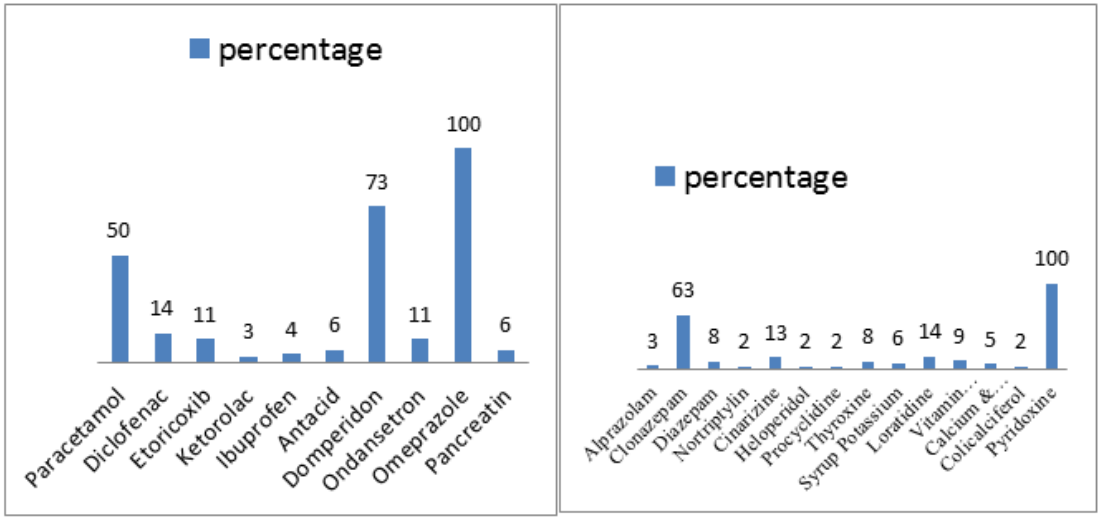

Fig-6: Distribution of respondents by Ancillary drugs used to manage Adverse Effects of MDR-TB drugs (n =64)

Among NSAIDs, in 60% (32/53) cases Paracetamol, in 17% (09/53) cases Diclofenac, in 13% (07/53) cases Etoricoxib, in 06% (03/53) cases Ibuprofen and in 04% (02/53) cases Ketorolac had been used.

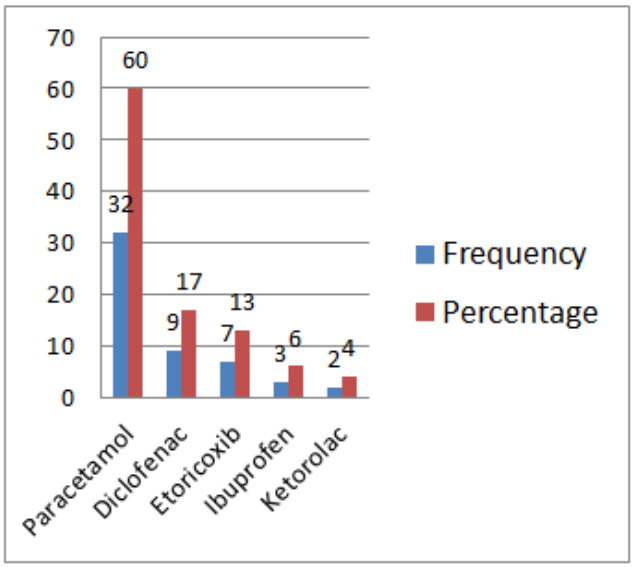

Fig-7: Distribution of respondents by NSAIDs used to manage Adverse Effects of MDR-TB drugs (n =53)

As antiemetic, Domperidon and Ondansetron had been used in 87% and 13% cases respectively. Antacid had been used in 6% (4/64) cases. Among the respondents with raised serum TSH level, Thyroxine had been prescribed in 42% (05/12) cases.

As anxiolytic Clonazepam had been used in 85% cases. Diazepam and Alprazolam had been used in 11% and 04% cases respectively to manage adverse effects of MDR-TB drugs.

Adverse effects had been attempted to be managed at NIDCH (National Institute for Diseases of the Chest & Hospital, Mohakhali, and Dhaka) in 100% (64/64) cases. 17% (10/64) had been referred to SAHIC (Society for Assistance to Hearing Impaired Children, Mohakhali, Dhaka) and 02% (01/64) each to NIKDU (National Institute for Kidney Diseases & Urology, Sher-e- Bangla Nagar, Dhaka) and NIMH (National Institute of Mental Health, Sher-e- Bangla Nagar, Dhaka).

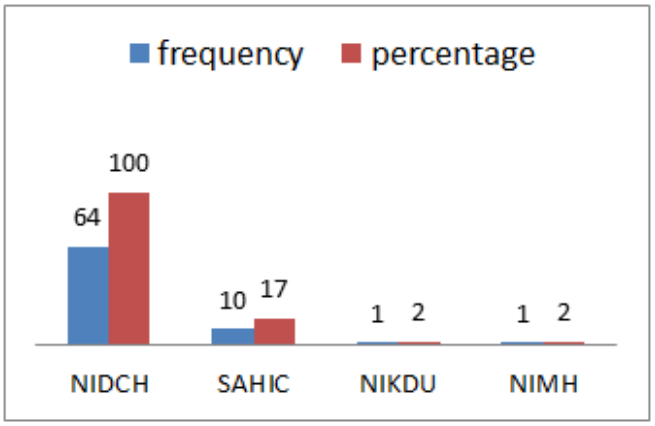

Fig-8: Distribution of respondents by place of management of Adverse Effects of MDR-TB drugs (n =64)

Impaired hearing developed in 17% (11/64) respondents and among them 91% (10/11) had been sent to ENT specialist of SAHIC.

Among the respondents with raised serum creatinine, in one patient each, offending drug dose had been reduced and had been stopped. For management of renal impairment one patient had been sent to NIKDU.

Table-2: Distribution of respondents by impaired hearing & place of management

Patients with impaired hearing (n=64)		Patients sent to SAHIC (n=11)	
Frequency	Percentage	Frequency	Percentage
11	17	10	91

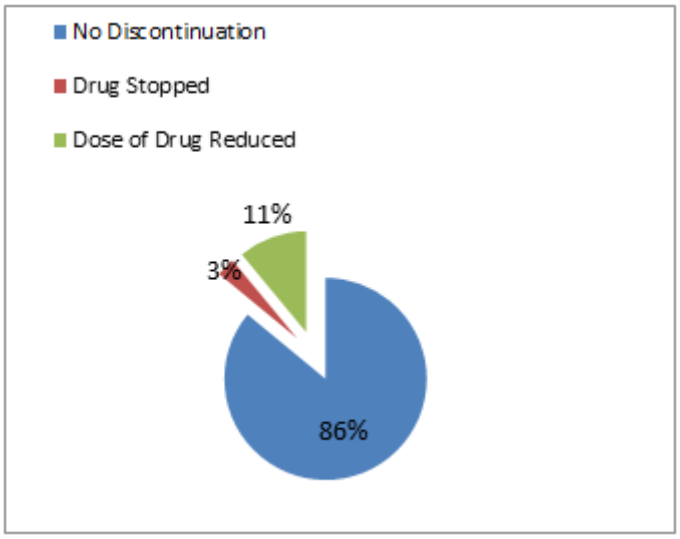

Fig-9: Distribution of respondents by discontinuation of MDR-TB drug (n=64)

Uninterrupted treatment had been continued in 86% (55/64) cases. Drug dose had to be reduced in 11% (07/64) cases and drug had to be stopped in 03% (02/64) cases.

DISCUSSION

The study reveals that the mean age of respondents was 34.76 ± 12.98 (mean±SD) years. 20-60 years age group comprised of 80% respondents, which indicates that the most valuable working period of life could not escape from the claw of MDR-TB and thus tuberculosis is affecting the main contributors of GDP [11]. Among the respondents, 66% were male and 34% were female with a male to female ratio of 2:1. Result shows that males are more commonly infected with MDR-TB than females. This trend is also observed in some other studies [6, 7, 12].

25% respondents were illiterate. Among female 36% were illiterate and none had graduation or higher degree indicating that regarding education women still lag behind. It was most alarming that 83% respondents did not complete the level of S.S.C. Highest 27% respondents were service holder. Among them 47% were garments worker and 12% had history of working abroad. In case of women 55% were house wives. The mean income of the working respondents was 10,859/- taka per month. 73% had monthly income below 10,000/- taka which indicates the low socioeconomic status of the patients. Study in Turkey suggests that 56.7% of MDR-TB cases occurred among those with poor economic status [13]. Result of population prevalence survey regarding TB in Bangladesh also showed that poor, less educated & worker class contribute to the higher prevalence of the disease [14].

In the study 61% and 33% people were married and unmarried respectively. But married people were not contaminated from their spouse though they could have been contaminated their healthy spouse. Among the respondents, 25% had history of contact with TB patients which mean that they were susceptible to TB. Again 11% were susceptible to MDR-TB and 3% had history of contact with both TB and MDR-TB patients. Most of them (39%) had contact with siblings, 26% with father, 9% with mother and 4% with offspring. 22% had contacts with others like uncle, mother-in-law, and roommates as well which indicates close contact that is living in same house hold or spending several hours per day together with the patient in same indoor living or working space [5]. The contact period was from 15 days to 1 year. Among male respondents 79% were smokers though smoking increases risk of infection, progression of TB and death [12]. None of the women was smoker and pregnant.

Regarding co-morbidities, 14% had been suffering from DM, 6% from Br. Asthma and 3% from COPD. All respondents were HIV negative & in First Bangladesh National Tuberculosis Drug Resistance Survey among 1468 respondents, 0.1% (only one) had been found HIV positive [7].

Regarding treatment of TB with 1st line anti-TB drugs 31% respondents (20/64) were not informed about the adverse effects but it occurred in 27% cases.

3% had history of discontinuation of treatment which was only temporary and the duration of interruption was 7 days to 14 days. In case of MDR-TB, all patients had been informed about the adverse effects of the drugs.

98% (63/64) cases had Pulmonary TB & rest had Extra Pulmonary TB and the site was cervical lymph node. In both cases treatment regimen was almost the same [5]. Among the respondents 28% belongs to relapse cat-I. 19% and 14% were from treatment failure cat-I and cat-II respectively. On the other hand relapse cat-II was 17%. Delayed converter group consisted of 14% of respondents. 3% belonged to the group of primary MDR-TB while incidence of MDR-TB among new cases is 1.4% in Bangladesh [7]. Among the primary cases one had the history of contact with MDR-TB patient but another had the history of contact neither with TB nor with MDR-TB patient.

As dosing of anti-TB drugs is based on the weight of the patients, monthly weight monitoring had been done. From base line to the end of 3rd month average weight gain (male 2 kg & female 1 kg) did not require to move into higher weight class to adjust the medication dose as well [5]. Again the mean weight of the patients (at baseline 39.77kg in female & 45.61kg in male) has indicated their poor nutritional status.

Regarding the adverse effects 80% (51/64) had suffered from arthalgia. Study in Canada also revealed the same type of finding (82%) [15]. Arthalgia and head ache had been managed by NSAIDs like Paracetamol, Diclofenac, Etoricoxib, Ibuprofen, Ketorolac etc. but uricosuric agents were not recommended. 59% had anorexia and 44% had nausea & vomiting. Study in China among 273 MDR-TB patients also found the occurrence of vomiting in 45% cases [16]. 28% suffered from peripheral neuropathy and among them 50% were diabetic and rest 50% were non diabetic. All respondents had been prescribed to take Pyridoxine from beginning of treatment and 9% was given vitamin B_1, B_6, B_{12} combination. Insulin had been used in all diabetic cases [7].

52% & 33% developed vertigo and tinnitus respectively.17% (11/64) developed impaired hearing and among them 91% (10/11) had been sent to nearby ENT specialist of SAHIC because there had no facility of specialized ENT care in NIDCH and otologist & audiologist have an important role in preventing irreversible hearing loss caused by MDR-TB drugs[17]. According to the advice of ENT specialist, dose of Kanamycin had been reduced in 11% (7/64) cases but serum level of the drug was not measured to evaluate whether the serum concentration of the drug was sufficient to kill the bacilli or not.

3% developed hepatitis which had been noticed through scheduled monitoring. But treatment was not interrupted as treatment would not be changed immediately only when ALT, AST, total bilirubin is elevated to greater than 2 times [16]. 3% developed nephrotoxicity. Due to high serum creatinine level after stopping Kanamycin, one patient had been referred to NIKDU for management of renal impairment as NIDCH had not the specialist support for nephrology and urology.

In spite of using Proton Pump Inhibitor (Omeprazole) in 100% cases, 19% (12/64) developed gastritis. Though antacid is advised to avoid, as they may decrease absorption of Flouroquinolones, in 6% cases it had been used [5]. Hypothyroidism was observed in 19% (12/64) cases. Among 12 hypothyroid patients, 05 were advised to take thyroxine. 44% and 19% respondents suffered from sleep disorders and psychological disorders like psychosis (8%), anxiety (25%), depression (67%) etc and fortunately none from suicidal ideation. As TB patients are perceived as a source of infection resulting in their social rejection and isolation, the disease & drugs lead to a long term impairment of their psychosocial wellbeing [13, 14]. Clonazepam was used most frequently (85%) as anxiolytic agent. One patient developed psychosis and Cycloserine had been stopped for 2 weeks and antipsychotic drug Haloperidol with Procyclidine was advised by physician of NIDCH. Though 67% had depression, they were not advised to take a newer antidepressant drugs and proper counseling was not arranged as NIDCH lacks of specialized psychiatry department. One patient had been referred to NIMH for depressive illness. None developed diarrhoea, impaired vision, muscle cramp, seizure etc.

Uninterrupted treatment had been continued for 1st 3 months in 86% (55/64) respondents. Dose of drug (Kanamycin) had to be reduced in 11% (07/64) and stopped in 3% (02/64) respondents. Cycloserine was stopped temporarily for 2 weeks and then re-introduced after improvement of sign symptoms of psychosis in case of one respondent [18]. During the study period after discontinuation, Kanamycin could not be reintroduced as sign symptoms and laboratory findings of nephrotoxicity were not adequately improved.

Limitations

Only the hospital admitted MDR-TB patients were included in the study. But those who had been treated at community level through cPMDT (Community Based Programmatic Management of Drug Resistant TB) could not be included. It was not mentioned whether the patient was smear positive or negative which would provide an idea regarding the severity of chance of spread of MDR-TB. Due to lack of facilities baseline audiometry was not done. To manage the adverse effects, dose of offending drug was reduced by physician. But whether the dose was sufficient to kill the bacilli was not monitored by

measuring the serum level of the drug. Patients were observed for 3 months only.

CONCLUSION

Treatment of MDR-TB requires prolonged therapy with multiple drugs which leads to adverse reaction in a significant number of patients. Adverse effects lead to treatment interruption, drug discontinuation and drug dose reduction. Proper counseling of patients, monitoring and management of adverse effects of drugs should be the components of attention towards the completion of anti-TB treatment. The findings of this study may provide baseline information in Bangladesh on adverse effects of MDR-TB drugs as well as a guide for designing and implementing appropriate and timely response once adverse effects are identified. The information may help minimizing the treatment interruption and thus prevent propagation and dissemination of MDR-TB.

The study finding recommends the establishment of specialized ENT, Nephrology and Psychiatry units in NIDCH, Dhaka. Further long term studies involving large number of MDR-TB patients (hospital admitted as well as treated under cPMDT programme) are needed to learn more about the adverse effects of MDR-TB drugs along with its management. Basic Pharmacological research and pharmacovigilance is needed to shed light on the treatment of MDR-TB so that the therapy could be continued in doses that will render effective drug level yet minimizing the adverse effects.

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