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Profile of Adverse Drug Reactions among Multi Drug Resistant Tuberculosis and Extensively Drug Resistant Tuberculosis Patients and To Assess Its Severity at Tertiary Care Centre of North India.

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Abstract

Context : Worldwide, Tuberculosis (TB) is one of the top 10 causes of death, and the leading cause from a single infectious agent. Globally in 2017, WHO estimated incidence of Rifampicin Resistant (RR) and multi drug resistant tuberculosis (MDR-TB) in India is estimated to be around 147000. This translates to around 11 patients per 100 000 population annually as per the Global TB Report, 2017 [1].

Aim and Objective: To study the Profile of Adverse Drug Reactions among Multi Drug Resistant Tuberculosis And Extensively Drug Resistant Tuberculosis Patients and To Assess Its Severity At Tertiary Care Centre Of North India.

Methods & Material: This study was a hospital based Prospective observational study in which 644 patients were taken over a period of February 2015 to September 2019, Data were collected from patients attending the Outpatient and Inpatient of the department of respiratory medicine fulfilling the inclusion and exclusion criteria and according to a predesigned proforma gathering clinical history, examination and investigations. Causality assessment and severity of adverse drug reaction were done as per World health organisation criteria. Standard statistical

averages, standard deviation and mean deviation were calculated.

Result: We evaluated a total of 644 patients of MDR TB and extensively drug resistant tuberculosis (XDR TB) for any adverse drug reaction(ADR) . Mean age of patients in our study was 43.7 ± 14.2 years. Out of 644 patients , 442 (68.60%) were male and 202 (31.40%) were females. A total of 316 (49.06%) patients among 644 patients were experienced 480 adverse drug reactions (ADRs) during their treatment with mean age 41.7 ± 9.2 years.

Conclusion: Among 480 ADRs, 57.91% of ADRs were of gastro intestinal system (most common) followed by 9.37% ADRs of nervous system. Out of 480 ADRs, 366 (76.25%) ADRs were possible, 101 (21.04%) probable and 13 (2.71%) were certain according to causality assessment by WHO criteria. Out of 480 ADRs, 258 ADRs (53.75%) of Grade I, 174 (36.25%) of Grade II, 40 (8.33%) of Grade III and 8 (1.67%) ADRs were of Grade IV Severity. In our study there were 20 (4.16%) such cases of ADRs where permanent discontinuation of offending drugs were done .

Keywords : MDR TB, XDR TB , Adverse drug Reaction

Summary : Worldwide, Tuberculosis (TB) is one of the top 10 causes of death, and the leading cause from a single infectious agent. The treatment of MDR-TB is challenging because of prolonged duration of therapy , significant drug toxicities and adverse drug reactions (ADRs). This study was a hospital based Prospective observational study in which 644 patients were taken over a period of February 2015 to September 2019. Causality assessment and severity of adverse drug reaction were done as per World health organisation criteria. A total of 644 patients of MDR TB and XDR TB were evaluated for any adverse drug reaction . A total of 316 (49.06%) patients among 644 patients were experienced 480 adverse drug reactions (ADRs) during their treatment under DOTS-plus therapy with mean age 41.7 ± 9.2 years. Among 480 ADRs, 57.91% of ADRs were of gastro intestinal system (most common) followed by 9.37% ADRs of nervous system. Out of 480 ADRs, 366 (76.25%) ADRs were possible, 101 (21.04%) probable and 13 (2.71%) were certain according to causality assessment by WHO criteria. Out of 480 ADRs, 258 ADRs (53.75%) of Grade I, 174 (36.25%) of Grade II, 40 (8.33%) of Grade III and 8(1.67%) ADRs were of Grade IV Severity. In our study there were 20 (4.16%) such cases of ADRs where permanent discontinuation of offending drugs were done.

Introduction

Worldwide, Tuberculosis (TB) is one of the top 10 causes of death, and the leading cause from a single infectious agent. Globally in 2017, there were an estimated 10.0 million incident cases of TB (range, 9.0–11.1 million), equivalent to 133 cases (range, 120–148) per 100 000 population. India contributes around 27% of global burden of TB. There were an estimated 558 000 new cases (range, 483 000–639 000) of rifampicin resistant TB (RR-TB), of which almost half were in three countries: India (24%), China (13%) and the Russian Federation (10%). WHO estimated incidence of Rifampicin Resistant (RR) and MDR-TB in India is estimated to be around 147000. This translates to around 11 patients per 100 000 population annually as per the Global TB Report, 2017 [1].

The treatment of MDR-TB is challenging because of prolonged duration of therapy, significant drug toxicities and adverse drug reactions (ADRs). Thus disease contributes to significant morbidity and

mortality which to a great extent is preventable by assuring adherence to guidelines and management of adverse drug reactions (ADRs). It is essential to monitor adverse drug effects in a systematic and timely manner. A comprehensive knowledge regarding patterns, severity, causative agents of a ADR need to be evaluated so that timely intervention can be done. ADR is one of the most important aspect to be understood by all those who used to involved in the management of tuberculosis , therefore this study was planned.

Aim

To study the Profile of Adverse Drug Reactions among Multi Drug Resistant Tuberculosis And Extensively Drug Resistant Tuberculosis Patients and To Assess Its Severity At Tertiary Care Centre Of North India.

Objectives

1. Identification of types and frequency of adverse drug reactions.

2. To assess causality and severity of the reported adverse drug reactions.

Material & Methods

This study was a hospital based Prospective observational study in which 644 patients were taken over a period of February 2015 to September 2019, done at respiratory medicine department of tertiary care centre of north India. Ethical clearance was taken from the institutional ethical committee.

During study period, patients >10 years of age receiving Multi drug resistant tuberculosis and extensively drug resistant tuberculosis treatment registered in DR-TB (Drug Resistant Tuberculosis Centre) Centre of a tertiary care centre were included in the study. Those patients who did not give consent, Pregnant, less than 10 years of age, transferred out, died and default their treatment were excluded from the study. Patients with deranged Liver and Kidney function tests and Other chronic disease condition requiring any concomitant medication were excluded. Those patients who were reported ADRs and managed at peripheral centres were also excluded in the study.

The Revised National TB Control Programme (RNTCP) has launched “Directly Observed treatment Short-Course (DOTS) Plus” for management of drug resistant tuberculosis (DR-TB) in 2007 and has expanded these services to all states and Union Territories across the country in 2012. RNTCP has taken the programmatic decision that patients who have any Rifampicin resistance, should also be managed as if they are an MDR TB case as rifampicin resistance is quite rare without isoniazid resistance. Standardized treatment regimen for MDR-TB under daily DOTS-Plus includes 6-9 months Intensive Phase (IP) drug therapy & 18 months Continuation Phase (CP) drug therapy. Intensive for XDR TB is 6 to 12 months and 18 months Continuation Phase (CP) drug therapy. (Table 1)

Table . 1 Drugs Used in MDR TB and XDR TB

S/N	Multi drug Resistant Tuberculosis		Extensively Drug Resistant Tuberculosis	
	Intensive Phase (6 ---9 month)	Continuation Phase (18 months)	Intensive Phase (6----12 months)	Continuation Phase (18 months)
1	Kanamycin	---------	Capreomycin	-------
2	Levofloxacin	Levofloxacin	Moxifloxacin	Moxifloxacin

3	Ethambutol	Ethambutol	Linezolid	Linezolid
4	Cycloserine	Cycloserine	High Dose Isoniazid	High Dose Isoniazid
5	Ethionamide	Ethionamide	Amoxyclav	Amoxyclav
6	Pyrazinamide	-----	Para Amino Salicylic Acid (PAS)	Para Amino Salicylic Acid (PAS)
7	-----	----	Clofazimine	Clofazimine
8.	Pyridoxine	Pyridoxine	Pyridoxine	Pyridoxine

Drug used as per standardized weight band (16—29 kg, 30—45 kg ,46—70 kg , > 70 kg) of RNTCP DOTS Plus Programme. (Table 2)

Table 2: Dosage of DRTB Drugs for Adult

S/N	Drugs	16-29 kg	30—45kg	46—70 kg	>70 kg
1.	High Dose Isoniazid (H^h)	300mg	600mg	900mg	900mg
2.	Ethmbutol	400mg	800mg	1200mg	1600mg
3.	Pyrazinamide	750mg	1250mg	1750mg	2000mg
4.	Kanamycin	500mg	750mg	750mg	1000mg
5.	Capreomycin	500mg	750mg	750mg	1000mg
6	Amikacin	500mg	750mg	750mg	1000mg
7.	Levofloxacin	250 mg	750 mg	1000mg	1000mg
8.	Moxifloxacin	200mg	400mg	400mg	400mg
9	Linezoloid	300mg	600mg	600mg	600mg
10	Amoxy clav	875 /125 mg	875 /125 mg BD	875 /125 mg 2 Morning + 1 Evening	875 /125 mg 2 Morning + 1 Evening
11	Clofazimine	50mg	100mg	100mg	200mg
12	Ethionamide	375mg	500mg	750mg	1000mg
13	Cycloserine	250 mg	500mg	750mg	1000mg
14	Pyridoxine	50mg	100mg	100mg	100mg
15	NA- PAS (60%weight / volume)	10gm	14gm	16gm	22gm

These MDR and XDR TB Cases require prolonged treatment using second line drugs which are highly toxic and less effective [2]. Any noxious or unintended response to a drug which occurs at doses normally used in human for the prophylaxis, diagnosed or treatment of disease or for the modification of physiological function is termed as Adverse Drug Reaction [3,4].

Data were collected according to a predesigned proforma regarding Age , Sex , Weight, Body Mass Index (BMI) ,Co-Morbid illness such as Diabetes

Mellitus, Hypertension, Dose and Duration Of MDR-TB and XDR TB Drugs, other medications, and ADR. Investigations such as Complete Blood Count, Liver Function Tests (LFT), Renal Function Tests (RFT), Serum Electrolyte, Electrocardiography and Random Blood Sugar, Fasting and Post Prandial Blood Sugar , Viral marker for hepatitis B (HBSAG) and hepatitis C(HCV) and testing for human immunodeficiency virus (HIV) , Chest X Ray were recorded.

Special Investigation

Computed Tomography Of Chest and Head

Nerve Conduction Velocity

Audiometry

Ophthalmoscopy

Ultrasonography Of Abdomen

Causality Assessment and Severity of Adverse drug reactions were done as per world health organisation Criteria [5,6,7] (Table 3).

Table 3: World Health Organisation Causality Categories

S/N	Causality Term	Assessment Criteria
1	Certain	1.Event or laboratory test abnormality, with plausible time relationship to drug intake Cannot be explained by disease or other drug 2.Response to withdrawal plausible (pharmacologically, pathologically) 3.Event definitive pharmacologically or phenomenologically (i.e. an objective and specific medical disorder or a recognised pharmacological phenomenon 4. Rechallenge satisfactory, if necessary
2	Probable	1.Event or laboratory test abnormality, with reasonable time relationship to drug intake 2.Unlikely to be attributed to disease or other drugs 3.Response to withdrawal clinically reasonable 4.Rechallenge not required
3	Possible	1.Event or laboratory test abnormality, with reasonable time relationship to drug intake 2.Could also be explained by disease or other drugs 3.Information on drug withdrawal may be lacking or unclear

Severity of adverse drug reactions were presented as grading ,There were 5 grades:-

Grade 1 Mild; asymptomatic or mild symptoms; clinical or diagnostic observations only; intervention not indicated.

Grade 2 Moderate; minimal, local or non invasive intervention indicated.

Grade 3 Severe or medically significant but not immediately life-threatening; hospitalization or prolongation of hospitalization indicated

Grade 4 Life-threatening consequences; urgent intervention indicated.

Grade 5 Death related to adverse event .

Data were entered into MS-Excel sheet**.** Descriptive statistics was used to analyze the data. Results were

expressed as either percentage or mean ± standard deviation (SD).

Results

We evaluated 644 MDR TB & XDRTB patients who were registered during the study period. There were 555 (86.18%) cases of MDR Pulmonary Tuberculosis and 30(4.65%) cases were MDR Extra Pulmonary Tuberculosis. There were 58 (9%) cases of XDR Pulmonary TB and 01 (0.15%) case of Extra Pulmonary XDR TB. Mean age of patients in our study was 43.7 ± 14.2 years. Maximum patients belongs to age group 20 to 39 years. Out of 644 patients 442 (68.60%) were male and 202 (31.40%) were females. (Figure 1)

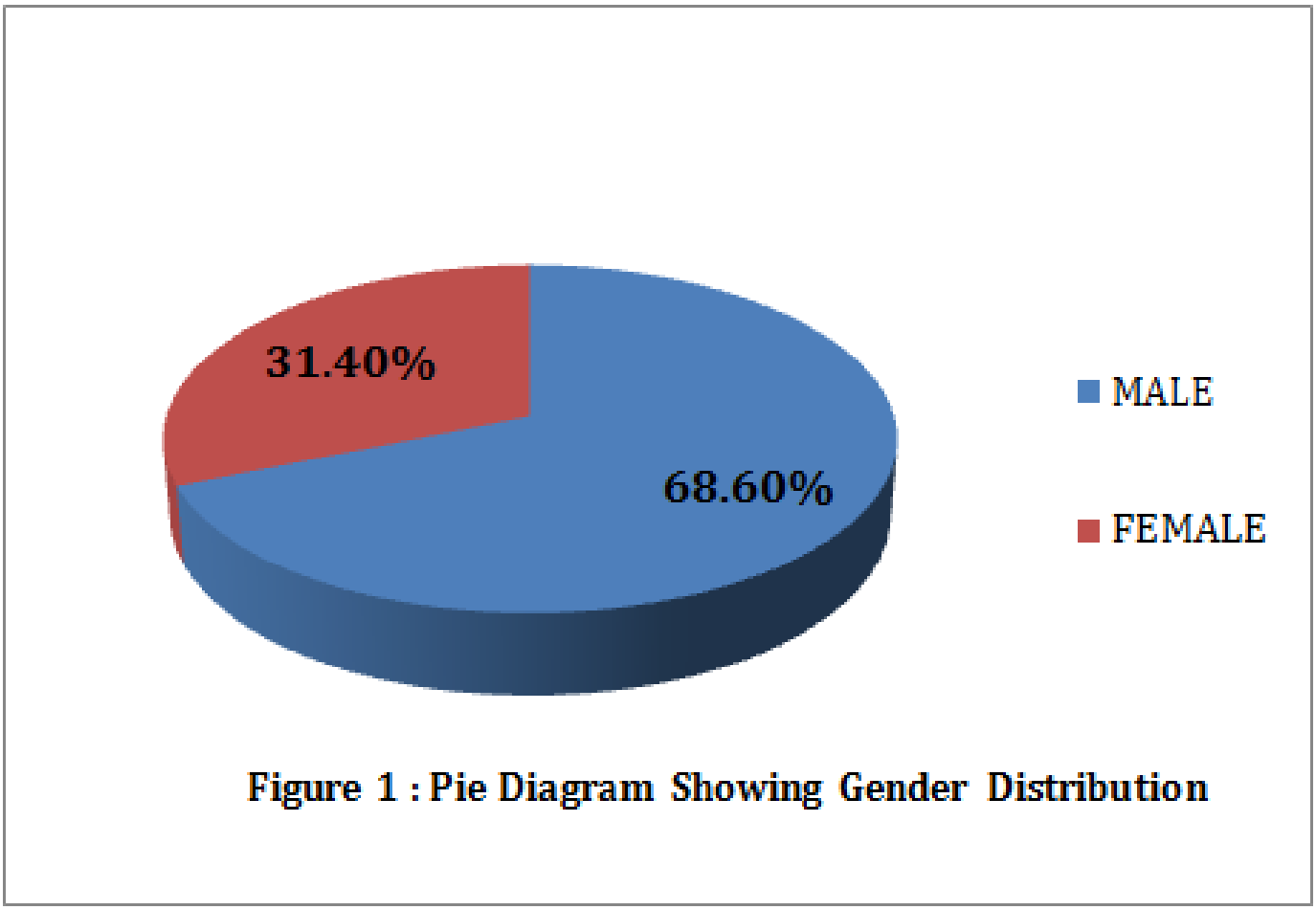

Figure 1 : Pie Diagram Showing Gender Distribution

Mean body weight of study population was 43.10±8.4 kg. Maximum patients 386 (59.93%) were belong to under nutrition as per Body Mass Index (BMI) (<18.5). (Table 4)

Table. 4 Demographic Profile of MDR TB and XDR TB Patients

Demographic Profile	Total n=644(%)	Cases with Adverse Drug Reaction (MDR TB +XDR TB)288 + 28 316 (%)	Cases with Adverse Drug Reaction (XDR TB) 28 (%)
Age Group (Years)			
10-19	77 (11.96)	45 (14.24)	02(7.14)
20-39	296(45.96)	143 (45.23)	13(46.42)
40-59	216(33.54)	106 (33.54)	9(32.14)
60-89	55 (8.55)	22 (6.96)	4(14.28)
Sex Male	 442 (68.60)	 220 (69.63)	 17(60.71)
Female	202 (31.40)	96 (30.38)	11(39.29)
Weight	43.10±8.4	41.10±6.3	44.10±7.3
Body Mass Index (BMI kg/m2)			
Under nutrition (<18.50)	386 (59.93)	192(60.75)	17(60.75)
Normal (18.50-24.90)	184 (28.55)	98(31.01)	09(32.14)
Pre obese (25-29.90)	42 (6.5)	18(5.6)	02((7.14)
Obese (>30)	32 (4.9)	8(2.5)	01(3.57)
New Case	48(7.4)	28(8.86)	2(7.15)
Retreatment Cases	596(92.54)	288(91.14)	26(92.85
MDR Pulmonary TB	555(86.18)	274(86.70)	0
XDR Pulmonary TB	58(9.00)	27(8.55)	27(96.43)
MDR Extra Pulmonary TB Cold abscess Pleural effusion Lymphadenitis	30(4.65) 05 (0.7) 16 (2.4) 09 (1.39)	14(4.43) 2(0.63) 9(2.84) 3(0.94)	0

XDR Extra Pulmonary TB (Cervical Lymphadenitis)	01(.15)	01(0.31)	01(3.57)

*** TB Tuberculosis , MDR Multi Drug Resistant , XDR Extensively Drug Resistant**

A total of 316 (49.06%) patients among 644 patients were experienced 480 adverse drug reactions (ADRs) during their treatment under DOTS-plus therapy with mean age 41.7 ± 9.2 years. Maximum 220 (69.60%) patients were belonged to male gender and female were 96 (31.40%). Among 28 patients of XDR Tuberculosis 44 Adverse Drug Reactions were found. (Figure 2, Table 5)

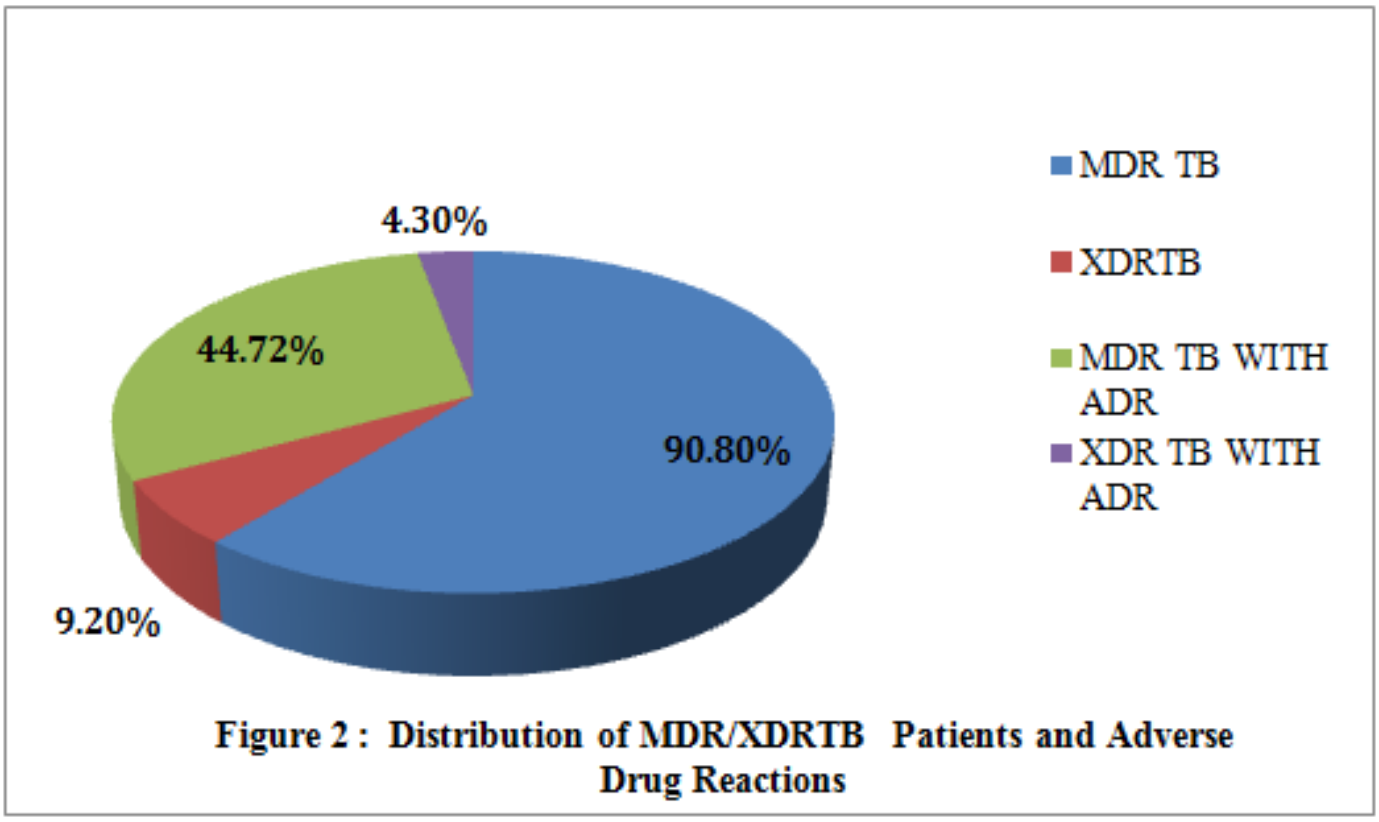

Figure 2 : Distribution of MDR/XDRTB Patients and Adverse Drug Reactions

Among 480 ADRs, Gastro Intestinal System 278 (57.91%) was most commonly affected system, 45 (9.37%) ADRs in Nervous System, 40 (8.34%) ADRs of Joint Pain, 36 (7.5%) ADRs in Oto Rhino Vestibular System, 37 (7.70%) ADRs of Hepatitis and 16(3.4%) ADRs of Nephrotoxicity were noted . ADRs reported related to Dermatological System and Ocular System were 16 (3.4 %) and 12 (2.5%) respectively.

Among ADRs of Gastrointestinal System, nausea & vomiting 176 (62.58%) was most common, abdominal pain 66 (23.74%) and diarrhoea was 38 (13.67%). Among ADRs of Nervous System, Depression 18(40%), Psychosis 10 (22.22%), Peripheral Neuropathy 6 (13.34%) and Suicidal Ideation

2(4.45%) were noted . Among ADRs of Otovestibular system, Ototoxicity 25 (69.45%), Vertigo 6 (16.66%) and Tinnitus 5 (13.88 %) were found . Hepatitis as adverse drug reaction seen as 37 (7.7%). Mean value of serum bilirubin 2.02 ± 0.55 mg % , SGPT (Serum Glutamic Pyruvic Transminase) 281 .58 ± 61.31 IU/L and SGOT (Serum Glutamic Oxaloacetic Transminase) 346.68 ± 53.04 IU /L were found where hepatitis reported as ADR.. .

Among ADRs of Dermatological System itching 9 (56.25%) was most common ADR. Among ocular ADRs blurring of vision 5(41.6%) was most common. In our study 20 (4.16%) cases of adverse drug reaction where permanent discontinuation of offending drugs were done and replacement of culprit drug was done by reserved drug (PAS). (Table 5)

Table 5: Incidence and Characteristic of Adverse Drug Reactions.

Adverse Drug Reaction (ADR)	Incidence MDR TB + XDR TB [n=480] (%)	Incidence XDR TB (%) (n=44)	Duration of treatment in days (Mean±SD)	Suspected Drugs	Permanent Discontinuation Of Drugs
Gastro Intestinal System	278 (57.91)	24 (54.55)	22 ± 17.3 17 ± 24 26 ± 28	Ethionamide/ Pyrazinamide/ Ethambutol/ PAS, Amoxyclav / Fluroquinolones/ Clofazimine/Isoniazid$^{H/}$	----------
Nausea & Vomiting Abdominal Pain Diarrohea	174 (62.58) 66 (23.74) 38 (13.67)	14 (58.33) 6 (25) 4 (16.67)			
Nervous System	45 (9.37)	2 (4.54)	26 ± 28	Cycloserine Ethionamide	05
Depression Psychosis Insomnia Headache Peripheral Neuropathy Suicidal Ideation	18 (40) 10 (22.22) 4 (8.89) 5 (11.11) 6 (13.34) 2 (4.45)	2 (100) 0 0 0 0 0	47.2 ± 26.4 9.42± 2.78 9.285± 2.85 95 ± 51.25 55		------ 03 ------ ------ ------ 02
Joint Pain	40 (8.34)	0	53 ± 52	Pyrazinamide / Fluroquinolones	-----
Hepatitis	37 (7.70)	6 (13.64)	24 ± 17	Pyrazinamide/ Ethionamide / PAS/ Isoniazid^{H}	-----

Otovestibular ADRs Ototoxicity Vertigo Tinnitus	36(7.5) 25 (69.45) 6 (16.66) 5 (13.88)	6 (13.64) 6 (100) 0 0	79.55± 48.9 68 .12 ± 64.04 16.4 ± 5.6	Kanamycin/ Capreomycin	 13 ---- ----
Nephrotoxicity	16 (3.4)	2 (4.54)	40 ± 12.25	Kanamycin/ Capreomycin	----
Dermatological ADRs Itching Skin Pigmentation Skin Rash	16 (3.4) 9 (56.25) 4 (25) 3 (18.75)	4 (9.09) 0 4 (100) 0	15.2 ± 4.6 47 ± 13.25 5.71 ±1.70	Pyrazinamide/ Ethambutol/ Isoniazid[H] Clofazimine Fluroquinolones	----
Ocular ADRs Blurring of Vision Vision loss Diplopia	12 (2.5) 5 (41.66) 4 (33.34) 3 (25)	0 0 0	45 ± 12.25 28± 15.6 50 ± 12.25	Ethambutol ,	---- 02 -----

*****TB : Tuberculosis , MDR: Multi Drug Resistant , XDR : Extensively Drug Resistant **,** PAS: Para-Amino salicylic Acid

Out of 480 adverse drug reactions, 366 (76.25%) ADRs were possible, 101 (21.04%) probable and 13 (2.71%) were certain according to causality assessment by WHO criteria. Out of 480 ADRs, 258 ADRs (53.75%) of Grade I, 174 (36.25%) of Grade II, 40 (8.33%) of Grade III and 8(1.67%) of Grade IV Severity by WHO criteria. (Table 6)

Table. 6: Causality Assessment and Severity Assessment of Adverse Drug Reactions

S/N	Adverse Drug Reaction [ADR] (n = 480)	WHO Casualty Assessment				Severity			
		No. of ADR	Certain	Probable	Possible	Grade 1	Grade 2	Grade 3	Grade 4
1	Gastro Intestinal	278							
	Nausea & Vomiting	174	0	63	111	126	33	11	4
	Abdominal Pain	66	0	12	54	51	13	2	0
	Diarrhoea	38	0	0	38	21	17	0	0
2	Central Nervous System	45							
	Depression	18	0	0	18	16	2	0	0

	Psychosis	10	0	0	10	4	6	0	0
	Insomnia	4	0	0	4	0	4	0	0
	Headache	5	0	0	5	1	4	0	0
	Peripheral Neuropathy	6	0	2	4	1	3	2	0
	Suicidal ideation	2	1	1	0	0	0	0	2
3	Joint Pain	40	0	0	40	0	34	6	0
4	Hepatitis	37	0	8	29	13	21	3	0
5	Otovestibular Adrs	36							
	Ototoxicity	25	12	7	6	3	8	12	2
	Vertigo	6	0	0	6	4	2	0	0
	Tinnitus	5	0	0	5	3	2	0	0
6	Nephrotoxicity	16	0	0	16	6	8	2	0
7	Dermatological ADR	16							
	Itching	9	0	0	9	4	5	0	0
	Skin Pigmentation	4	0	4	0	0	3	1	0
	Skin Rash	3	0	0	3	2	1	0	0
8	Ophthalmological ADR	12							
	Blurring of Vision	5	0	2	3	3	2	0	0
	Diplopia	3	0	0	3	0	3	0	0
	Vision loss	4	0	2	2	0	3	1	0

Discussion

In our study of 644 patients age groups ranged were 10 to 89 years. Maximum number of cases 296 (45.96%) were in age group of 20 to 39 years followed by 216 (35.54%) cases belonged to 40 to 59 age group. The mean age of patients in our study was 37.6 years comparable to previous studies [8]. The percentage of male patients (68.60%) greater than female 202 (31.40%) similar findings were seen our studies [8,9,10].

Mean body weight of patients in our study was 43.10 +8.4 kg and 386 (59.93%) patients belonged to under nutrition, similar finding observed in other studies [8,10]. Out of 644 patients, ADRs were seen in 316 (49.06%) patients similar findings also seen in another studies [11,12].

Total adverse drug reactions (ADRs) in our study were 480, out of 480 ADRs 436 ADRs were seen in MDR TB patients and 44 ADRs were seen in XDR TB patients. Most common system involved in ADRs was gastrointestinal system , out of 480 ADRs 280 (57.91%) were of gastro intestinal system, similar findings found in other studies as well and suspected drugs were Ethionamide, Pyrazinamide, Ethambutol, Para Aminosalicylic Acid (PAS) and Isoniazid (in high dose) [8,11,12,13,14] , most of the Adrs of gastro intestinal system belonged to Grade 1 severity , permanent discontinuation was not done in any cases.

Second most common system affected by ADRs was nervous system which accounted for 45 (9.37%). Among ADRs of CNS, there were depression (40%), psychosis (22.22%), peripheral neuropathy (13.34%), headache (11.11%), insomnia (8.89%) and suicidal ideation (2.25%). The common offending drugs were cycloserine, fluroquinolone and ethionamide. Higher rates of psychosis and depression in previous studies in also [13, 15] . All patients with psychosis required replacement of cycloserine with PAS during their psychosis phase afterwards cycloserine was reintroduced with antipsychotic treatment. Two patients who had suicidal ideation cycloserine was permanently discontinued in these patients .

Third most common Adverse drug reaction in our study was joint pain in 8.34%, similar findings were also reported in past [16]. Pyrazinamide and Fluroquinolones and can cause arthralgia. Hepatitis was seen in 37(7.70%) as ADRs , suspected drugs were Pyrazinamide ,Isonazid ^{H}, Ethionamide, Pyrazinamide ,PAS.

Otovestibular System contributed 36 (7.5%) ADRs among adverse drug reactions. Among 36 adrs ototoxicity were 25(69.45%), Vertigo 6 (16.66%), Tinnitus 5 (13.88%), The suspected drugs were kanamycin and capreomycin. There was very high rate of ototoxicity 41.8% was reported by Tourn et al, could be attributed to higher doses and extended exposure to aminoglycosides[16]. In 11 cases of ototoxicity dose of aminoglycosides were reduced and given alternatively and in 13 cases aminoglycosides were permanently discontinued .

Renal involvement was seen 16 (3.40%) patients in this study which is similar to observation noted in different other studies 2.7% and 2% respectively [11,12] . Renal involvements were seen in the form of borderline derangement of serum creatinine (1.95±.54 mg%), serum urea (75.2±.16.70) which improved in few weeks and none required permanent withdrawal of injection Aminoglycosides . Dermatological ADRs were 16 (3.4%), among dermatological ADRs, itching 9 (56.25%), skin pigmentation 4 (25%) and skin rashes 3 (18.75%), similar observation was found in other studies [8, 10, 11]. Ocular ADRs were 12 (2.5%), among ocular ADRs blurring of vision 5 (41.6%), vision loss 4 (33.34%) and diplopia 3 (25%), similar findings supported by other studies [12].

Conclusion

In our study adverse drug reactions were found in 316 ((49.06%) patients. Among 480 ADRs, 57.91% of ADRs were of gastro intestinal system (most common) followed by 9.37% ADRs of nervous system. Out of 480 ADRs, 366 (76.25%) were possible, 101 (21.04%) probable and 13 (2.71%) were certain according to causality assessment by WHO criteria. Out of 480 ADRs, 258 ADRs (53.75%) of Grade I, 174 (36.25%) of Grade II, 40 (8.33%) of Grade III and 8(1.67%) ADRs were of Grade IV Severity. In our study 20 (4.16%) cases of adverse drug reaction where permanent discontinuation of offending drugs were done.

Limitation

This study did not include those MDR TB and XDRTB patients who have comorbid conditions like diabetes , hypertension and HIV etc and those MDRTB patients who were kept on shorter regimen and those MDR TB with additional resistance patients and XDR TB patients who were started on bedaquiline containing regimen.

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