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ADVERSE DRUG REACTIONS CAUSED DUE TO ANTITUBERCULAR DRUG THERAPY IN PATIENTS RECEIVING FIRST LINE TREATMENT - A RETROSPECTIVE OBSERVATIONAL STUDY

Rajesh Bhaskar Nawale*[1], P. S. Jirvankar[2], Nikita Anil Kantak[1], Aishwarya Atul Badhe[1], Ankita Ashok Kirdak[1], Tanvi Sharad Mathurvaishya[1]

[1]Government College of Pharmacy, Aurangabad. 431 005, Maharashtra, India.
[2]Associate Professor, Medicine Department, Govt. Medical College and Hospital, Aurangabad 431 005, Maharashtra, India.

***Corresponding Author: Rajesh Bhaskar Nawale**

Government College of Pharmacy, Aurangabad. 431 005, Maharashtra, India.

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ABSTRACT

Tuberculosis (TB) is a communicable infectious disease caused by *Mycobacterium tuberculosis (M. tuberculosis)*. India accounts for 1/4th of global TB burden. Primary infection of TB is initiated by the alveolar implantation of organisms in droplet nuclei. General signs and symptoms include fever, chills, night sweats, loss of appetite, weight loss, and fatigue. Significant finger clubbing may also occur. Treatment with anti Tb agent induces significant adverse drug effects which might remain unreported. The retrospective observational study was carried out in 65 patients; suffering from tuberculosis receiving first line treatment from In-patient department (IPD) in Tertiary Care Hospital at Aurangabad The primary objective of study includes monitoring patients for ADRs. The secondary objective of study is to counsel patient about means to decrease effects to improve adherence. Detailed history was taken regarding the demographic profile, present complaints, past history of TB, history of any addiction, family history of TB. Detailed general and systemic examination was done to find out any abnormalities. Form the study it was concluded that the majority of adverse drug reactions observed were mild and includes gastro-intestinal upset (nausea, vomiting and abdominal pain). There was no marked sign of hepatotoxicity. Special intervention and knowledge to cure these mild adverse effects can lead to increased patient compliance.

KEYWORDS: Tuberculosis, Adverse drug reactions, Antitubercular drug, Retrospective observational study.

INTRODUCTION

Tuberculosis (TB) is a communicable infectious disease caused by *Mycobacterium tuberculosis (M. tuberculosis).* It can produce silent, latent infection as well as progressive, active disease. TB usually affects Lungs, but can involve any part of the body. Extra-pulmonary TB can affect Lymph nodes, pleura, bones, joints, genitourinary tract, nervous system (meninges, tuberculomas), abdominal organs (intestines, mesentery, solid organs), skin, etc. The life risk of breaking down to disease those among infected with TB is 10 to 15 %. Other determinants such as diabetes mellitus, smoking, tobacco products, alcohol abuse and malnutrition also increases the risk of progression from infection to TB disease.[1]

Primary TB is uncommon type of TB presents as pneumonia and is very infectious. Patients have a high fever and productive cough. It occurs most often in extremely young children and the elderly. It is also seen in patients with immune-suppression, such as people with HIV/AIDS, and in patients on long term corticosteroid therapy. Pleural effusion is usually develops soon after initial infection. A granuloma located at the edge of the lung ruptures into the pleural space. Once the bacteria invade the space, the amount of fluid increases dramatically and compress the lung. Cavitary TB involves the upper lobes of the lung. The bacteria cause progressive lung destruction by forming cavities, or enlarged air spaces. The upper lobes of the lung are affected. Cavitary TB can rarely occur soon after primary infection. Occasionally, disease spreads into the pleural space and causes TB empyema (pus in the pleural fluid). Patients who are immune-suppressed and children who have been exposed to the bacteria are at high risk for developing miliary TB. TB bacteria cause death of tissue in the organs they infect. Active TB disease can be fatal if left untreated.[2]

Multidrug-resistant tuberculosis (MDR-TB) has resistance to at least isoniazid and rifampicin. India is one of the high burden countries for TB as well as drug-resistant TB. As per WHO's "Global Tuberculosis

Report, 2012", India account for an estimated 64000 patients out of 310000 cases of Drug Resistant TB estimated to have occurred amongst the notified cases of TB across the globe in a year.[3] Extensive drug resistant tuberculosis (XDR-TB) has resistance to at least isoniazid and rifampicin (i.e. MDR-TB) plus resistance to any of the fluoroquinolones and any one of the second-line injectable drugs (amikacin, kanamycin, or capreomycin). Drug-susceptible TB and XDR TB are spread the same way. XDR-TB is resistant to the most potent TB drugs, the remaining treatment options are less effective, have more side effects, and are more expensive. XDR-TB is of special concern for persons with HIV infection or other conditions that can weaken the immune system. These persons are more likely to develop TB disease once they are infected, and they also have a higher risk of death if they develop TB disease. Some TB control programs have shown that cure is possible for an estimated 30% to 50% of affected people. Successful outcomes depend greatly on the extent of the drug resistance, the severity of the disease, whether the patient's immune system is weakened, and adherence to treatment.[4] Extremely drug resistant tuberculosis (XXDR-TB) is totally drug resistant TB (TDR-TB), is TB which is resistant to all the first and second line TB drugs. This makes it almost but not totally impossible to treat. This term was 1st time used in 2007. The TDR-TB patients remained smear positive after 18 months median treatment despite second line drugs. Treatment with drugs like Coamoxiclav (625 mg/8 hrs.) or Clarithromycin (1000 mg/day) along with high dose of Isoniazid (15 mg/kg) also does not show any improvement.[4] Rifampicin resistant tuberculosis (RR-TB) is caused by TB bacteria that do not respond to rifampicin, one of the most effective anti-TB medicines, requiring longer treatment and more medication than patients with rifampicin-susceptible disease.[3]

Research in Tuberculosis

On March 24, 1882, when Robert Koch completed his presentation on the infectious cause of tuberculosis. A means of combating TB a disease that in the 19th century caused, by some accounts, about 25% of all deaths in Massachusetts and New York and claimed the lives of one fourth of Europe's population was now within reach. Koch summarized the importance of his findings, for which he received the 1905 Nobel Prize.

In 1943, that the first effective anti-TB agent, streptomycin, was isolated in the laboratory of Selman Waksman at Rutgers University. In November 1944, a patient with TB received streptomycin and was declared cured of the disease. The British Medical Research Council conducted the first large-scale clinical trial of streptomycin in 1948. This study, said to be the world's first published drug trial that involved the randomization of participants, set the methodological standard for modern randomized, controlled trials. Although many patients were cured, a substantial proportion had a relapse; mycobacterial isolates cultured from the latter patients showed resistance to streptomycin. That same year, two new antituberculosis agents, thiacetazone and P-aminosalicylic acid, came on the market.

Table 1: Alternative method of grouping anti TB agents.

Group 1	First line oral anti-TB agents	Isoniazid, Rifampicin, Ethambutol , Pyrazinamide
Group 2	Injectable anti-TB agents	Streptomycin, kanamycin, Amikacin, Capreomycin, Viomycin
Group 3	Fluoroquinolones	Ciprofloxacin, Ofloxacin, Levofloxacin, Moxifloxacin, Gatifloxacin
Group 4	Oral second line anti TB agents	Ethionamide, Prothionamide, Cycloserine, Terizadone, Para amino salicylic acid
Group 5	Agents with unclear efficacy	Clofazimine, Linezolid, Amoxicillin/Clavulanate, Thioacetazone, Imipenem/Cilastatin, High dose Isoniazid, Clarithromycin.

When either of these agents was administered with streptomycin, cure rates rose and acquired antibiotic resistance declined. In 1951, isonicotinic acid hydrazide (isoniazid) was tested at Sea View Hospital in New York; it dramatically improved clinical outcomes and was soon introduced for wider use. Isoniazid was followed by the development of pyrazinamide (1952), cycloserine (1952), ethionamide (1956), rifampin (1957), and ethambutol (1962).

With its high level of efficacy and ease of administration, rifampin revolutionized the treatment of tuberculosis. But the advent of every new drug led to the selection of mutations conferring resistance to it. Resistance to rifampin was observed soon after it was first administered.

Table 2: Dosage and weight band recommendations.

Sr. No.	Drugs	16 to 25 kgs	26 to 45 kgs	> 45 kgs
1	Kanamycin	500 mg	500 mg	750 mg
2	Ofloxacin (Levofloxacin)	400 mg (200 mg)	600 mg (500 mg)	800 mg (750 mg)
3	Ethionamide	375 mg	500 mg	750 mg
4	Ethambutol	400 mg	800 mg	1000 mg
5	Pyrazinamide	500 mg	1250 mg	1500 mg
6	Cycloserine	250 mg	500 mg	750 mg
7	PAS	5 gm	10 gm	12 gm
8	Pyridoxine	50 mg	100 mg	100 mg

Table 3: New TB drugs under clinical developments.

Phase 1	Phase 2	Phase 3
Q203-Novel anti-TB agent Imidazopyridine	Sutezolid (PNU-100480) Oxazolidinone	Bedaquiline (TMC207) with OBR for MDR-TB Diarylquinoline OBR = Optimized Background Regimen
	SQ109 Ethylenediamine	Delamanid (OPC-67683) with OBR for MDR-TB Nitro-dihydro-imidazooxazole
	Rifapentine for DS-TB Rifamycin	Pretomanid –Moxifloxacin-Pyrazinamide New chemical entity
	Bedaquiline – Pretomanid – Pyrazinamide	
	Levofloxacin Fluoroquinolone	

Incidence and Epidemiology

India accounts for 1/4th of global TB burden i.e. 2.2 million out of 9.6 million new cases annually. In India, more than 40% of populations have prevalence of infection with TB. It is estimated that there are 2.5 million prevalent cases of all forms of TB disease. It is also estimated that about 2.2 lakh people die due to TB annually (mortality).

Table 4: TB burden globally and for India by WHO 2014.

	Incidence	Prevalence	Mortality
Global	9.6 million (176/lakh/year)	13 million (227/lakh/year)	1.1 million (21/lakh/year)
Indian	2.2 million (167/lakh/year)	2.5 million (195/lakh/year)	2.2 lakh (17/lakh/year)

TB now ranks alongside HIV as leading cause of death worldwide. TB kills more adults in India than any other Infectious Disease. In India every day more than 6000 develop disease and more than 600 people die of TB.[1]

PATHOPHYSIOLOGY

Primary infection is initiated by the alveolar implantation of organisms in droplet nuclei that are small enough (1 to 5 mm) to escape the ciliary epithelial cells of the upper respiratory tract and reach the alveolar surface. Once implanted, the organisms multiply and are ingested by pulmonary macrophages, where they are killed, or, they continue to multiply. With bacterial multiplication, the macrophages eventually rupture, releasing many bacilli.

Successful containment of *M. tuberculosis* requires activation of a subset of CD4 lymphocytes. This activates macrophages through secretion of interferon. Approximately 90% of patients who experience primary disease have no further clinical manifestations other than a positive skin test either alone or in combination with radiographic evidence of stable granulomas. Tissue necrosis and calcification of the originally infected site and regional lymph nodes may occur, resulting in the formation of a radiodense area referred to as a Ghon complex. Approximately 5% of patients experience progressive primary disease at the site of the primary infection (usually the lower lobes). Approximately 10% of patients develop reactivation disease, which arises subsequent to the hematogenous spread of the organism.[6]

Signs and Symptoms

TB may infect any part of the body, but most commonly occurs in the lungs (known as pulmonary TB). Extra pulmonary TB occurs when TB develops outside of the lungs, although extra pulmonary TB may coexist with pulmonary TB as well. General signs and symptoms include fever, chills, night sweats, loss of appetite, weight loss, and fatigue. Significant finger clubbing may also occur.

Pulmonary symptoms: Early symptoms and signs are often nonspecific and insidious, consisting mainly of

diurnal fever and night sweats due to defervescence, weight loss, anorexia, general malaise, and weakness. However, up to 90% of cases, cough eventually develops often initially non-productive and limited to the morning and subsequently accompanied by the production of purulent sputum, sometimes with blood streaking. Hemoptysis develops in 20 to 30% of cases, and massive hemoptysis may ensue as a consequence of the erosion of a blood vessel in the wall of a cavity. Hemoptysis, however, may also result from rupture of a dilated vessel in a cavity (Rasmussen's aneurysm) or from aspergilloma formation in an old cavity. Pleuritic chest pain sometimes develops in patients with sub pleural parenchymal lesions or pleural disease.

Systemic features include fever (often low grade and intermittent) in up to 80% of cases and wasting. Absence of fever, however, does not exclude TB. In some cases, pallor and finger clubbing develop. The most common hematologic findings are mild anemia, leukocytosis, and thrombocytosis with a slightly elevated erythrocyte sedimentation rate and/or C-reactive protein level. None of these findings is consistent or sufficiently accurate for diagnostic purposes. Hyponatremia due to the syndrome of inappropriate secretion of antidiuretic hormone has also been reported.[7]

Extrapulmonary: In 15 to 20% of active cases, the infection spreads outside the lungs, causing other kinds of TB. These are collectively denoted as extra pulmonary TB. Extra pulmonary TB occurs more commonly in immune-suppressed persons and young children. In those with HIV, this occurs in more than 50% of cases.
Notable extra pulmonary infection sites include the pleura (in TB effusion), the central nervous system (in tuberculousmeningitis), the lymphatic system (in scrofula of the neck), the genitourinary system (in urogenital tuberculosis), TB keratitis and the bones and joints (in Pott's disease of the spine), among others. When it spreads to the bones, it is also known as "osseous TB" a form of osteomyelitis. Sometimes, bursting of a tubercular abscess through skin results in tuberculous ulcer. An ulcer originating from nearby infected lymph nodes is painless, slowly enlarging and has an appearance of wash leather,[8,9]

LITERATURE REVIEW

Daphne Yee et al (Jan2003) performed a retrospective cohort study in 430 patients. Incidence of serious side effects from first line anti tuberculosis drugs among the patients treated for active tuberculosis was studies and conclusion were most striking. Finding was the common occurrence of major adverse reactions due to pyrazinamide. Incidence of pyrazinamide induced hepatotoxicity and rash was significantly higher than for the other first line anti TB drugs.[10] Amit R. Dedun et al (March 2017) conducted prospective observational study in 974 patients of range 20 to 75 years. Impact of ADRS of 1st line antituberculous drugs for treatment of TB under RNTCP was studies. Higher incidences of ADRs were found in age group of 31 to 40 ages. Occurrence of ADRs were more in male patients (63%) as compare to female (37%).[11] Omaima Eibouazzi et al (Nov 2016) conducted retrospective study in 142 patients. This comprises of study on first line anti TB drugs induced hepatotoxity incidence and risk factors. The mean age for the patient in the study was 42.6 years. Amongst them 14 (9.9%) of alcoholism and 56 (39.4%) were smokers, 35 (24.6%) of all patients developed hepatotoxicity. Apart from hepatotoxicity, patient developed other adverse effects on TB treatment that includes: Extrapulmonary as a whole general disorder (6.3%), GI Disorders (10.6%), psychiatric disorder (1.4%), vascular bleeding &clotting disorders (2.1%) and metabolic disorder (0.7%) [12]. Horita N, et al. (2015) conducted randomized study in 195 patients for study of drug induced liver injury during pyrazinamide use. The incidence of drug induced liver injury in the first two months was 15 %. [13]. Russo PA, Chaglasian MA (May 1994) conducted randomized study in 120 cases for observation of toxic optic neuropathy associated with ethambutol and its implications of current therapy. They concluded that ethambutol is implicated in development of visual related side effects.[14] Prassad R et al. (2008) observed 110 cases under observational studies for isoniazide and ethambutol induced psychosis. Most of the cases treated with anti TB drugs are associated with psychosis. These psychosis patients were taking isoniazide. Ethambutal associated psychosis was rare [15]. Faith Yakaret, et al (2013) performed observational study in 96 patients to study isoniazide and rifampicin induced thrombocytopenia. They concluded that the patients have recurrent episodes of thrombocytopenia due to isoniazide and rifampicin, 2.5% of normal population has lower than 150000/mm^3 cell count [16]. Banu Eris Gulbay (Oct 2005) handled 1149 cases in retrospective study for primary side effects of anti TB drugs during initial phase of TB. They found that 95 patients (8.3%) experience side effects. 56 (4.9%) develop hepatotoxicity, ototoxicity in 20 (1.7%) patients, neuropsychiatric manifestation in 8 (0.7%) patients, hyperuriceamia in 7 (0.6%) patients, nausea, vomiting, abdominal pain in 782 (68%) and itchy skin rash in 173 (15%)patients, stiffness of muscle in 7 (0.6%), numbness in 13 (1.81%), thrombocytopenia in 1 (0.10%) patient [17]. Sahoko Chiba et al. (2013) conducted observational case study in 50 patients for study of rifampicin induced acute kidney injury during the initial treatment for pulmonary tuberculosis. They found suspected rifampicin induced kidney injury and also all patient present with proteinuria.[18] Showkat Ali Zargar et al (Oct 1999) in their retrospective study in 76 patients for rifampicin induced upper gastrointestinal bleeding found that the cause and effect relationship between development of hemorrhagic gastric erosions and rifampicin administration was confirmed by rechallenge with rifampicin.[19]

MATERIAL AND METHODOLOGY

The present study conducted during the period of December 2016 to March 2017, was a retrospective observational study in 65 patients, suffering from tuberculosis receiving first line treatment from In-patient department (IPD) in Tertiary Care Hospital at Aurangabad (Government Medical College and Hospital, Aurangabad, Maharashtra, India). The primary objective of study includes monitoring patients for ADRs, study ADRs amongst TB patients on first line Anti tubercular drugs and frequency of occurrence. The secondary objective of study is to counsel patient about means to decrease effects to improve adherence.

Exclusion criteria

- Patients who were receiving second line Anti tubercular drug treatment.
- Defaulter
- Patients who were receiving Anti Retro Viral Therapy.
- MDR and XDR tubercular patients.
- Non consenting Patients.

Clinical Evaluation & Procedures

Patients for this study were included from all patients diagnose to have TB admitted in tertiary health care hospital. Prior permission of institutional ethics committee was accorded. All study subjects were evaluated after written informed consent. Thorough detailed history was taken regarding the demographic profile, present complaints, past history of TB, history of any addiction, family history of TB. Detailed general and systemic examination was done to find out any abnormalities. Body mass index (BMI) was calculated in all the patients. The body mass index (BMI) is a measure for human body shape based on an individual's mass and height. The WHO regards a BMI of less than 18.5 kg/m^2 as underweight while a BMI greater than 25 kg/m^2 are considered overweight and above 30 kg/m^2 are considered obese.

Table 5: Normal BMI Range.

Category	BMI range – kg/m^2
Very severely underweight	less than 15
Severely underweight	from 15.0 to 16.0
Underweight	from 16.0 to 18.5
Normal (healthy weight)	from 18.5 to 25
Overweight	from 25 to 30
Obese Class I (Moderately obese)	from 30 to 35
Obese Class II (Severely obese)	from 35 to 40
Obese Class III (Very severely obese)	over 40

Pre-treatment investigations were done, which includes sputum for acid fast bacilli (AFB) by smear, culture and Chest X-ray, urine for albumin, sugar and complete haemogram, renal and liver function test.

Treatment regimen: The treatment regimen includes Isoniazid (H), Rifampicin (R), Pyrazinamide (Z), Ethambutol (E). The initial phase should consist of 2 months of drug HRZE. The continuation phase should consists of 2 drugs are Isoniazid, Rifampicin, given for at least 4 months. This is alternatively written as 2 HREZ / 4-6 HRE. In special situation the continuation phase may be extended by 3 to 6 months. The drug dosage was given accordingly body weight of the patient. All patients were monitored daily for adverse drug reactions after starting regimen till the patients remains admitted in hospital and later followed up personally or telephonically at regular intervals. Intense health education was given to the patients, along with family members, by doctors, nursing staff. Follow-up sputum cultures reports were obtained from the register maintained at tertiary health care center.

Findings were recorded on computer with Microsoft Excel 2010. No statistical test could be applied as per senior statisticians, as this is an observational study without controls maintained at tertiary health care center.

RESULTS

In the present study of 65 patients, the age group ranged from 17 to 84 years. Maximum no. of case was reported in the age group 21 to 39 were 33 (50.76%) followed by age group 40 to 59 were 20 (30.76%). The patients with age up to 20 years were only 3 (4.62%) and with age more than 60 were 9 (13.85%). Out of 65 participants majority of patients i.e. 50 (76.92%) were male and 15 (23.08%) were female.

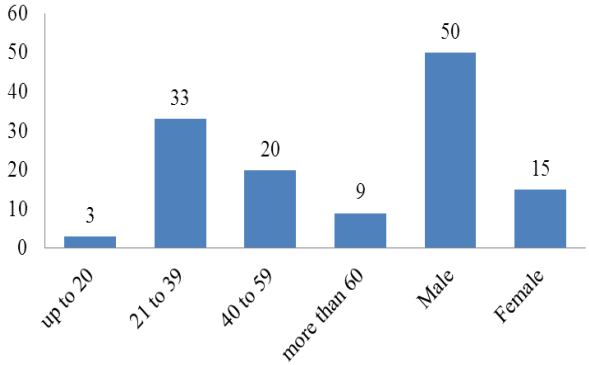

Fig. 1: Age and gender distribution of the participated patients.

Table 6: Adverse drug effects reported.

Sr. No.	Adverse effects	No. of patients	Percentage
1	ADRs observed in Patients	56	86.15
2	ADRs not observed in Patients	09	13.85
3	Nausea	25	38.46
4	Vomiting	11	16.92
5	Abdominal pain	10	15.38
6	Itchy skin rash	07	10.77
7	Stiffness of muscle	00	00
8	Hepatotoxicity	03	4.61
9	Thrombocytopenia	00	00
10	Loss of vision	01	1.54
11	Numbness	10	15.38
12	Decrease urine output	00	00
13	Behavioral changes	03	4.61
14	Impaired hearing	00	00

In the present study, patients developed ADRs in 56 (86.15%) patients and 9 (13.85%) patients does not report any ADR. Out of 65 patients 25 (38.46%) were observed to have nausea. vomiting in 11 (16.92%) patients. Abdominal pain and numbness was reported by 10 (15.38%) each, itchy skin rash by 7 (10.77%) and hepatotoxicity and behavioral changes in 3 (4.61%) each patients. Loss of visions reported by 1 (1.54%) patient, and none of the patients reported to have thrombocytopenia, decreased urine output, and impaired hearing.

The distribution of BMI is as per below table no. 7.

Table 7: Body mass index of the patients under investigation.

Sr. No	BMI	No. of patients
01	Very severe underweight (<15)	00
02	Severe underweight (15-16)	02
03	Underweight (16-18.5)	15
04	Healthy weight (18.5-25)	32
05	Overweight (>25)	13
06	More than 30	03

No very sever underweight patient was present in study. Sever underweight (BMI 15 to 16) patient were 2 (3.08%), underweight (BMI 16 to 18.5) patients were 15 (23.08%). Maximum patients were having normal healthy weight which were 32 (49.23%) followed by 13 (20%) overweight and 3 (4.62%) patients with more than 30 BMI.

DISCUSSION

The present study has evaluated a newly diagnosed tubercular patient with special reference to adverse drug reactions (ADRs) of drugs in which standard treatment of newly diagnosed tubercular cases.

Table 8: Comparative study between our and Amit R. Dedun, et al.

Criteria	Present study		Author's study Amit R. Dedun, et al (2017)	
	No. of patients	percentage	No. of patients	Percentage
Age Upto 20	03	4.61	107	13.30
Age 21 to 39 years	33	50.76	497	59.75
Age 40 to 59 years	20	30.76	295	23.5
Age more than 60 years	09	13.84	75	5.20
Male	50	76.92	613	62.94
Female	15	23.08	361	37.06

When compared with previous study by Amit R. Dedun et al. (2017) in 974 patients with this study in 65 patients. The highest occurrences of ADR reporting were in age group of 21 to 39 (50.76% in this study and 59.75% in study conducted by Amit R. Dedun, et al), followed by age group of 40 to 59 years of age. The occurrence of ADRs in teen age and geriatric patients is minimal. Similarly previous study by Amit R. Dedun, et al. (2017)

concluded that the occurrence of ADRs were more in male patients 62.94% as compare to female patients were 37.06% while in present study occurrence of ADRs in male patients is 76.92% and in female patient it is 23.08%.

Table 9: Comparative study between our and Banu Eris Gulbay (Oct 2005).

Adverse drug reaction	Present study (%)	Authors study (%) Banu Eris Gulbay (Oct 2005)
Nausea	38.46	68.00
Vomiting	16.92	
Abdominal pain	15.38	
Itchy skin rash	10.77	15.00
Stiffness of muscle	00	00.61
Hepatotoxicity	04.61	04.90
Thrombocytopenia	00	00.10
Loss of vision	01.54	00
Numbness	15.38	01.81
Decrease urine output	00	00
Behavioral changes	04.61	00.70
Impaired hearing	00	01.70

In the present study, patients developed ADRs due to anti-tubercular drug therapy are observed in the following percentage Nausea 38.46%; Vomiting 16.92%; abdominal pain 15.38%. Previous study by Banu Eris Gulbay Oct 2005 concluded that 68.00% patients reported nausea, vomiting and abdominal pain. Itchy skin rash was occurred in 10.77% patients in our study and Banu Eris Gulbay reported that 15% patients. Occurrence of stiffness of muscle, thrombocytopenia, loss of vision, decrease urine output, impaired hearing were negligible in both studies. Hepatotoxicity occurrence is almost similar in both studies. Present study indicates higher percentage of occurrence of numbness and neuropsychiatric manifestation (15.38% and 4.61%) as compared to study by Banu Eris Gulbay which reported in as 1.81% and 1.7% respectively.

CONCLUSIONS

This study was conducted on the patients of newly diagnosed tuberculosis from 4 nearby districts, admitted in tertiary health care system during the period of December 2016 to March 2017. The present study has evaluated the Demographic and clinical profile of newly diagnosed tubercular patient, time to sputum culture conversion, clinical outcomes of patients after completion of study and observes ADRs in these patients. The age group ranged from 15 years to 84 years, Majority of cases were male (76.92%), maximum number of patients (50.76%) were from age group of 20 to 39, and 65 Patients were on AKT. Out of total 65 patients 3.23 % were alcoholic, 20% were smokers and 3.23% were tobacco chewers, 3.07% were underweight with BMI <18.5 kg/m2, with median BMI of 17.2kg/m2. At the end of study we conclude that maximum (70.76%) ADRs reported were nausea, vomiting and abdominal pain followed by numbness (15.38%) and itchy skin rash (10.76%). Hepatotoxicity and behavioral changes were found in 4.61% patients each and loss of vision in 1.53% patients. Occurrence of Stiffness of muscle, thrombocytopenia, decreased urine output, impaired hearing were not observed.

It concludes that the majority of adverse drug reactions observed in patients taking anti TB treatment were mild and includes gastro-intestinal upset (nausea, vomiting and abdominal pain). This might be the primary cause to leave the treatment. There was no marked sign of hepatotoxicity. Special intervention and knowledge to cure these mild adverse effects can lead to increased patient compliance. More studies should be conducted to evaluate what leads to treatment failure and decreased compliance rate among patients. Studies should be conducted to evaluate the benefits of palliative care for TB patients. Efforts should be made to treat the adverse drug reactions and also provide emotional support to the patients.

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