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POST-TREATMENT COMPLICATIONS AMONG DRUG RESISTANT TUBERCULOSIS PATIENTS IN TERTIARY CARE SETTINGS

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Abstract
Despite major social and medical interventions around the sphere, tuberculosis is still a global health concern from many decades. Drug resistant tuberculosis is more difficult to treat further advent of adverse effects on completion of treatment compromise the quality of life. Patients infected with drug resistant TB are more prone to get toxic effects of chemotherapeutic drugs. Some of the adverse effects are long lasting and chronic. Aim of this study was to observe the adverse effects and complications of drug resistant TB patients on completion of their treatment at programmatic management of drug resistant TB (PMDT) site in a tertiary care hospital. This cross sectional study was undertaken at PMDT site of a well-known tertiary care hospital of Lahore Pakistan from February 2021 to January 2023. All the patients of drug resistant TB completing their treatment from PMDT site were interviewed to ask about complications and adverse effects. Ethical permission for this work was obtained and data was collected on predesigned questionnaire then entered and analyzed in SPSS. A total of 150 drug resistant TB patients were interviewed, consisting of 83 (55.3%) males and 67 (44.7%) females. An overall mean age of patients was remained to be 34.59±14.95 years. Joint pain (32.7%) was the most common complication reported by drug resistant TB patients followed by Nausea (32.0%) and vomiting (23.3%). Irreversible hearing loss (3.3%) and vision problems (2.7%) were also reported. Drugs to treat resistant TB cases keep higher level of toxicity as 79.3% of the study subjects had at least one complication. Male gender and long treatment group acquired significantly higher level of complications as compared to female gender and short term group respectively.

Keywords: Tuberculosis, Drug Resistant, Complications, Adverse Effects, Tertiary care.

Introduction

Contagion tuberculosis (TB) instigated by *Mycobacterium tuberculosis* (MTB) is transmittable via respiratory contact. Primarily MTB affects the lungs but may damage any of the organ and tissue including bones. Despite major social and medical interventions around the sphere, TB is still a global health concern from many decades. [1] Number of newly diagnosed patients has been surged to 7.5 million in 2022 was highest ever since 1995 when World Health Organization (WHO) taken up the monitoring of TB. [2] Pakistan ranks 5th regarding overall population equivalent to 2.99% of the global load and ranks same 5th highest TB burden country, perhaps carrying almost double 5.77% of total TB patients in the world. [2]

After invention of anti-TB drugs it was presumed to eradicate the disease from world in late 80's however emerging drug resistance and multidrug resistance heaved in early 90's posed a great challenge to global healthcare. Although disease infects every organ of body in every age group however studies evidenced to trust that younger population is at higher risk of acquiring drug resistant TB. [3] Poor dietary habits are also considered to lessen the level of immunity especially in age groups of 10-25 years. [4] Factors like delayed diagnosis, inadequate or inappropriate drugs, poor compliance and absence of moral or social backing contribute to emerge the drug resistance. Same factors are also associated with poor treatment outcomes like failure, relapse and other complication including death. [5]

Drug resistant TB is more difficult to treat especially in countries like Pakistan already suffering economic challenges and scarcity of resources further advent of adverse effects on completion of treatment compromise the quality of life. [6] Limited spectrum of available treatment options for drug resistant TB on the other hand is also a dilemma to recover from this superimposed infection thus increasing the hurdles of healthcare system in the world. [1] Most of TB Therapeutic agents are bacteriostatic and require particular stage to attack MTB. Isoniazid is known to inhibit cell wall synthesis of bacteria, [7] Rifampicin inhibits DNA dependent RNA polymerase of bacteria, [8] Ethambutol is thought to inhibit arabinosyl transferase enzyme required in cell wall synthesis, [9] Pyrazinamide requires Pyrazinoic acid released by bacilli to get activation and inhibits the enzyme fatty acid synthase-I in return. [10]

Treatment of TB is difficult as even treatment of drug sensitive TB requires at least six months particularly in pulmonary cases because of slow growing infectious agent. Further difficulties increase in treatment of drug resistant, multi drug resistant and extensively drug resistant TB cases. Patients infected with drug resistant TB are more prone to get toxic effects of chemotherapeutic drugs according to their category of treatment. Some of the adverse effects are long lasting and chronic while rest may be temporary. Keeping above in view present study was undertaken to observe the adverse effects and complications of drug resistant TB patients on completion of their treatment at programmatic management of drug resistant TB (PMDT) site in a tertiary care hospital.

Methods

This cross sectional study was undertaken at National Institute of Health - Health Research Institute TB Research Centre in collaboration to PMDT site of a well-known tertiary care hospital of Lahore Pakistan from February 2021 to January 2023. All the patients of drug resistant TB completing their treatment from PMDT site were interviewed to ask about complications and adverse effects.

Ethical permission for this work was granted by the Institutional Review Board through letter no. 439/RC/KEMU dated July 4, 2020. An informed consent was taken before data collection and a predesigned Performa was used for this purpose. Demographic information, age, gender, body mass index, education, area of residence and socio-economic status were noted. Histories like previous TB treatment, smoking, any addiction, diabetes and other medical conditions were recorded. Adverse reactions included loss of hearing, vision issue, irritation, joint pain, lethargy, unusual bleeding and trembling of hands etc. were noted. Further complications during treatment like abdominal pain, anxiety, arthralgia, constipation, dry cough, depression, diarrhea, dyspepsia, fits, nausea, vomiting, headache, neuropathy, psychosis deposes, Titus and vertigo were also asked. Treatment file of each patient was carefully checked to observe if the complications were reported or not.

Data was entered and analyzed by using special package for social sciences (SPSS) software v. 20.0. Continuous variables like age and body mass index were presented in terms of mean ± standard deviation and categorical variables like gender, histories, adverse reactions and complications were presented in terms of frequency and percentage. Complications were compared in terms of treatment categories and gender using chi square test and p value <0.05 was considered as significant.

Results

A total of 150 drug resistant TB patients were finally interviewed on completion of their treatment consisting of 83 (55.3%) males and 67 (44.7%) females presenting a female to male ratio of 1:1.24 in this study. An overall mean age of patients was remained to be 34.59±14.95 years where mean age of male patients as 35.98±14.44 years remained higher as compared to 32.87±15.49 years of female patients. A total of 52 (34.7%) patients were illiterate and only 7 (4.7%) had education above high school as shown in Figure 1. Similarly highest number of patients were from district Lahore followed by adjacent districts as depicted in figure 2.

Figure 1: Level of Education

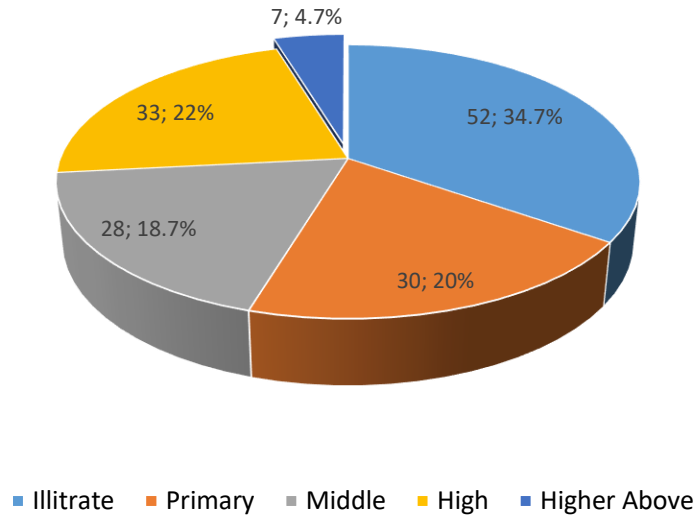
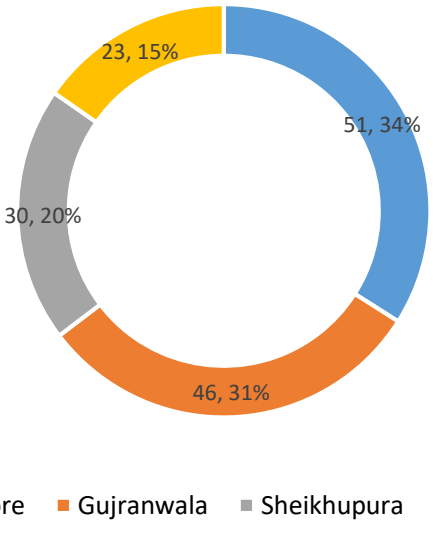
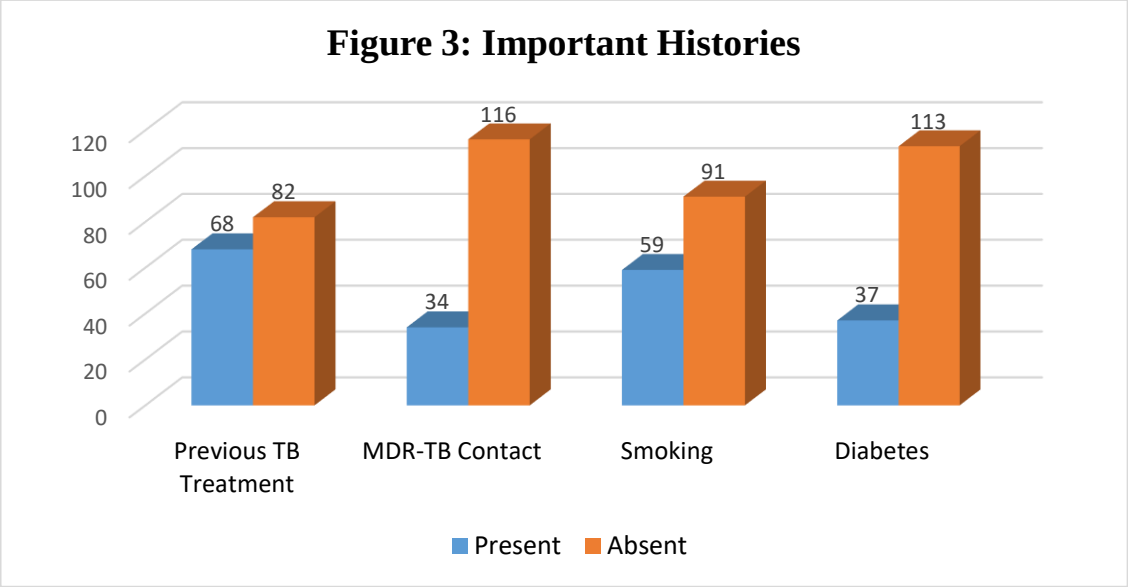


Figure 2: District of Residence





Joint pain was the most common complication reported by drug resistant TB patients followed by Nausea and vomiting. No trembling of hands, swelling of face and ankles, unusual bleeding and bloody or cloudy micturition was reported by the respondents in this study. All the complications their frequencies are presented in Table 1.

A total of 119 (79.3%) patients had at least one or more complications. Various characteristics were segregated in relation to these complications. Male gender is more prone to complications as compared to females (p-value <0.05) similarly short term treatment group showed less complications as compared to long term treatment group. Marital status, history of TB treatment and history of diabetes showed insignificant difference (p-value >0.05) as presented in Table 2.

Table 1: Complications During and at Completion of Treatment

Complications	Gender				Total (N=150)	
	Male (n=83)		Female (n=67)			
	n	%	n	%	n	%
Hearing Loss	2	2.4	3	4.5	5	3.3
Vision Problem	2	2.4	2	3.0	4	2.7
Nausea	26	31.3	22	32.8	48	32.0
Irritation	3	3.6	7	10.4	10	6.7
Weakness and Lethargy	7	8.4	5	7.5	12	8.0
Joint Pain	28	33.7	21	31.3	49	32.7
Abdominal Pain	2	2.4	0	0.0	2	1.3
Anxiety	0	0.0	4	6.0	4	2.7
Arthralgia	3	3.6	4	6.0	7	4.7
Constipation	1	1.2	0	0.0	1	0.7
Cough	1	1.2	0	0.0	1	0.7
Depression	8	9.6	11	16.4	19	12.7
Diarrhea	2	2.4	1	1.5	3	2.0
Dyspnea	2	2.4	2	3.0	4	2.7
Fits	0	0.0	2	3.0	2	1.3
Headache	4	4.8	9	13.4	13	8.7
Nausea	2	2.4	0	0.0	2	1.3
Neuropathy	8	9.6	3	4.5	11	7.3
Psychosis Deposes	3	3.6	0	0.0	3	2.0
Titus	0	0.0	5	7.5	5	3.3
Vertigo	2	2.4	5	7.5	7	4.7
Vomiting	16	19.3	19	28.4	35	23.3

Table 2: Segregation of Characteristics versus Complications

Characteristics		Complication				Total		p-value
		Yes		No				
		n	%	n	%	n	%	
Gender	Male	61	51.3	22	71.0	83	55.3	0.049
	Female	58	48.7	9	29.0	67	44.7	
Treatment Category	Short Term	49	41.2	23	74.2	72	48.0	0.001
	Long Term	70	58.8	8	25.8	78	52.0	
Marital Status	Married	75	63.0	17	54.8	92	61.3	0.404
	Unmarried	44	37.0	14	45.2	58	38.7	
History of TB Treatment	Present	55	46.2	13	41.9	68	45.3	0.670
	Absent	64	53.8	18	58.1	82	54.7	
History of Diabetes	Present	31	26.1	6	19.4	37	24.7	0.639
	Absent	88	73.9	25	80.6	113	75.3	

Discussion

Drug resistant TB patients face many treatment related challenges also that affect the quality of these patients. Most particularly these complications include nausea, hearing loss, and compromised capacity of routine activities of daily life. Stoppage of premature drug resistant TB treatment or default from treatment has been reasoned due to chemotherapeutic side effects. [11] On the other hand a recent literature has accentuated the rise in drug resistant TB as extremely challenging to manage. Since the frequency of resistant TB strains is alarmingly high amongst Pakistani people because of insufficient awareness regarding its easy respiratory transmission, poor treatment compliance, and lack of practicing the preventive measures in general. [1]

At present Joint Pain (32.7%), nausea (32.0%) and vomiting (23.3%) were the most communal complications among drug resistant TB patients. On the other hand mean age of patients was remained to be 34.59±14.95 years where mean age of male patients as 35.98±14.44 years remained higher as compared to 32.87±15.49 years of female patients. An important question brought ahead by the aging society is to see the impact of age on innovation, adaptation and productivity of individuals. Long living standards could only be achieved by the improvements in productivity while small changes in capacity at certain level show a great positive or negative impact in long run. There are few difference in disciplines, though most of the scientific literature is agreed on ages between 30 and 40 years are the most productive in life of any individual. [12] Mean ages of both genders revolve around the mean productive age and issues like joint pain and other complications are enough to compromise the future of these patients even they recover from disease.

Depression is reported to be in 12.7% patients at present, similar anxiety as 2.7% and psychosis deposes as 2.0% are few of the neurologic disorders reported in this study which also affect the quality of life greatly. These findings are in agreement to the study which reported these neurologic side effects along hepatitis, renal toxicity and auditory toxicity. Further neurologic side effects were reported to show less favorable outcomes along higher risks of death. [13] This phenomenon is not reported in present study and therefore a limitation at present. Another recent study showed a far different findings which presented 56% psychiatric illness among on treatment drug resistant TB patients.[14]

Although social stigma and depression are common among TB patients but tallying of drug resistance poses a great risk not only for the life of patient but also enhance the global challenge to control TB. The association amongst drug resistant strains of TB, stigma and depression on the other hand are not very well evaluated yet. [15] Therefore TB with multidrug resistant TB were reported to have 18.7% higher proportion as compared to drug susceptible TB patients. Similarly mean depression scores in drug resistant TB cases remained higher as compared to drug susceptible cases. [15] Present study also second the findings of above study. Few permanent disabilities like hearing loss and vision problem due to toxicity of anti-TB drugs are also important to consider and needs awareness

campaigns to opt the preventive measures especially people directly exposed and living with patients suffering from active infection.

Conclusion

Drugs to treat resistant TB cases keep higher level of toxicity as 79.3% of the study subjects had at least one complication in this study. Male gender and long treatment group acquired significantly higher level of complications as compared to female gender and short term group respectively. Few common complications like trembling of hands, swelling of face and ankles, unusual bleeding and bloody or cloudy micturition were not reported by the patients in this study.

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Conflict of Interest: Authors declare no any conflict of interest.

Ethics Approval: Ethical approval for this study was obtained from Institutional Review Board of King Edward Medical University and it is certified that study was performed in accordance with ethical standards as laid down in 1964 Declaration of Helsinki and its later amendments.

Author's contribution: All authors have significant contribution in this study. MKM & SR conceived the idea and designed the project, SR, AA and MAN collected the data and search the literature, MKM, AA and IA wrote the paper, AyA and AA observed the clinical relevance of data, SR and MAN revised the manuscript, MKM and AA did the data analysis, AyA and SR Wrote the results, Editing was completed by IA.

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