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THE FREQUENCY OF SUCCESSFUL OUTCOME OF MULTI-DRUG RESISTANT TUBERCULOSIS TREATED AS OUTPATIENT IN A TERTIARY CARE CENTER

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Abstract:

Tuberculosis [TB] remains one of the biggest health problems in developing and industrialized countries and is associated with high rates of morbidity and mortality. The emergence and spread of Mycobacterium tuberculosis strains resistant to multiple drugs represent a serious threat to TB control worldwide.[1]The estimated prevalence of MDR among new cases was 1.8% and 6.7% among previously treated cases. The estimated number of new MDR-TB cases annually was 8,000.[2]Early diagnosis of active TB and detection of multidrug-resistant [MDR] strains are essential to interrupt transmission.[3]Treatment adverse events, pill burden, rigidity of DOT, psychosocial support and interaction with health personnel pose major challenges to adherence for concomitant anti-TB and antiretroviral treatments.[4, 5]

Objectives: *To determine the frequency of successful outcome of multi drug resistant tuberculosis treated as outpatient in a tertiary care center.*

Subject and Methods: *This was a descriptive cross sectional study done from 13 April, 2018 to 13 OCT, 2018.All the patients fulfilling inclusion criteria having age 20-60 years of either gender under treatment of MDR-TB for more than six months were enrolled in study the from Programmatic Management of Drug Resistance Tuberculosis [PMDT] site at Department of Pulmonology. Informed consent was taken from patients. Strictly exclusion criteria i.e. patients having neurological or psychological problems before diagnoses of MDR-TB [as per medical record in history], co-infection with HIV, was followed to exclude potential confounder and biases. Education status was evaluated & response of treatment was checked in matriculate & under matric patients, also socioeconomic status was evaluated by asking about monthly salary whether below or above 12000, & subsequently their effect on treatment outcome. HIV screening done through ICT method & DST for tuberculosis done on sputum of the patients in Provincial Reference Lab in Hayat Abad Medical Complex Peshawar for diagnosis.*

Results: *Total of 151 patients were included in this study, among which males were 94 and females were 57. Mean age was 41 years and S.D 10.82. As per results, 110 [72.84%] patients were having successful outcome. [Table No. 6].*

Conclusion: *This study concludes that out-patient treatment strategy success rate was 72.84%% and it is feasible and safe for the treatment of MDR-TB patients.*

Keywords: *Tuberculosis [TB], Programmatic Management of Drug Resistance Tuberculosis [PMDT], Multidrug-resistant [MDR] strains.*

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INTRODUCTION:

Tuberculosis [TB] remains one of the biggest health problems in developing and industrialized countries and is associated with high rates of morbidity and mortality. The emergence and spread of Mycobacterium tuberculosis strains resistant to multiple drugs represent a serious threat to TB control worldwide.[1]The estimated prevalence of MDR among new cases was 1.8% and 6.7% among previously treated cases. The estimated number of new MDR-TB cases annually was 8,000.[2]Early diagnosis of active TB and detection of multidrug-resistant [MDR] strains are essential to interrupt transmission.[3]Treatment adverse events, pill burden, rigidity of DOT, psychosocial support and interaction with health personnel pose major challenges to adherence for concomitant anti-TB and antiretroviral treatments.[4, 5]

Management of multidrug-resistant TB [MDR-TB] patients is highly challenging. Such patients are subject to long and potentially toxic treatments and may develop a number of different psychiatric illnesses such as anxiety and depressive disorders. A mental health assessment before MDR-TB treatment initiation may assist in early diagnosis and better management of psychiatric illnesses in patients already having two stigmatizing and debilitating diseases.[6]A study shows 51 patients [96.2%] had pulmonary while 3 patients [5.6%] had extra-pulmonary TB. History of exposure to tuberculosis patients was found in 36 [67.9%] patients. Treatment regimen with 2nd line drugs was decided on individual basis according to DST on sputum culture results. The mean duration of treatment was 18 months. Successful outcome was seen in 25 patients [47.2%], 25 patients [47.2%] were loss to follow up and defaulted while 3 [5.6%] patients remain smear positive at the end of treatment.7Success rate was 89 .2% in those who completed the treatment. Treatment of MDR-TB is resource intensive and lasts for 24 months or more, requiring a combination of second-line drugs that are more expensive, less effective and more toxic than those used in standard first-line treatment regimens [8,9]. The cure including response rate of MDR-TB without human immunodeficiency virus [HIV] infection using individual tailored regimens was reported from 39% to 96 % in initially hospitalized patients. [10-14]

Aim of the study is to obtain fresh data with newer drugs that are provided free of cost to the patients by Government through PMDT [Programmatic Management of Drug Resistant TB] centers, and are not available in market. All tests are done free of cost. It will improve patient's compliance to medications and ultimately successful outcome as most patients previously lost follow-up as well as treatment due to high financial burden. That will benefit as patients will rely more on government health centers with better results. And ultimately control of the disease. Local data mostly is old while international data is having small sample size due to low disease burden there and not representative of our population due to difference in socioeconomic conditions and living standards.

Objective: To determine the frequency of successful outcome of multi drug resistant tuberculosis treated as outpatient in a tertiary care center.

MATERIAL AND METHODS:

This Cross sectional descriptive study conducted at Department of Pulmonology, Benazir Bhutto Hospital Rawalpindi from 1st February, 2020 to 30th July, 2020. sample size was 151 by taking the Prevalence of successful outcome 89%, CI=95% and margin of error .05 as determined by WHO Calculator. [7] Sampling Technique was non-probability, consecutive sampling.

Inclusion Criteria:

Patients of age 20-60 years of either gender under treatment of MDR-TB for more than 6 months.

Exclusion Criteria:

- Patients previously having neurological or psychological problems before diagnosis of MDR-TB [as per medical record and history]
- Co-infection with HIV which was confirmed by ICT method for the screening of HIV.

Data Collection Procedure:

All the patients fulfilling inclusion criteria having age 20-60 years of either gender under treatment of MDR-TB for more than six months were enrolled in study from Programmatic Management of Drug Resistance Tuberculosis [PMDT] site at Department of Pulmonology. Informed consent was taken from patients. Strictly exclusion criteria i.e. patients having neurological or psychological problems before diagnoses of MDR-TB [as per medical record in history], co-infection with HIV, was followed to exclude potential confounder and biases. Education status was evaluated & response of treatment was checked in matriculate & under matric patients, also socioeconomic status was evaluated whether below poverty line or above by asking about monthly salary whether below or above 12000, & subsequently their effect on treatment outcome. Screening for HIV was done through ICT method & DST for tuberculosis done on sputum of the patients in Provincial

Reference Lab in Hayatabad Medical Complex Peshawar for diagnosis.

Data Analysis Procedure:
All the collected data was entered into SPSS version 20 and analyzed through it. Quantitative data like age, salary and duration of MDR-TB was presented as mean and standard deviation. Qualitative data like gender, salary categories, education level, and successful outcome was presented as frequency and percentage. Chi square test was applied for the distribution of dependent variable [successful outcome of TB] with different independent variable like gender, salary categories, education level. Successful outcome was stratified for age, gender and duration of MDR-TB treatment to control effect modifier. Post stratification analysis was done through Chi square test while keeping P-value≤0.05 was taken as significant for the entire analytical test.

RESULTS:
This study was carried out on 151 patients at the Department of Pulmonology, Benazir Bhutto Hospital Rawalpindi. Results are appended:- As per descriptive statistics, mean and SD for age was recorded as 41 years + 10.82 and mean and SD for duration of MDR-TB was recorded as 8 months + 0.56. [Table No. 1]. As per age wise distribution, see [Table No. 2]. As per gender wise distribution, see [Table No. 3]. As per socio economic status, see [Table No. 4]. As per education level of patients, see [Table No. 5]. As per successful outcome, see [Table No. 6]. Stratification of successful outcome with respect to age and gender are recorded at Table No. 7 and 8.

TABLE NO. 1: Descriptive Statistics [N=151]

Quantitative Variables	MEAN	SDs
Age	**41 Years**	**10.82**
Duration of MDR-TB	**8 Months**	**0.56**

TABLE NO. 2: Age and Gender Distribution, Monthly Income, Education Level [N=151]

Age Group	**20-40 Years**	69	45.69%
	41-60 Years	82	54.30%
Gender	**Male**	94	62.25%
	Female	57	37.74%
Monthly Income	**< Rs 12,000/-**	59	39.07%
	≥ Rs 12,000/-	92	60.92%
Education Level	**Non Matric**	55	36.42%
	Matric	96	63.57

TABLE NO. 6: Frequency and Percentages for Successful Outcome [N=151]

Successful Outcome	Frequency	Percentage
Yes	110	72.84%
No	41	27.15%
Total	**151**	**100%**

TABLE NO. 7: Stratification of Successful Outcome with Age [N=151]

Age	Successful Outcome	Frequency	Percentage	P value
20-40 Years	Yes	61	40.39%	0.0909
	No	08	05.29%	
41-60 Years	Yes	49	32.45	
	No	33	21.85%	

TABLE NO. 8: Stratification of Successful Outcome With Gender [N=151]

Gender	Successful outcome	Frequency	Percentage	P value
Male	Yes	76	50.33%	
	No	18	11.92%	
Female	Yes	34	22.51%	0.680
	No	23	15.23%	

DISCUSSION:

It is estimated 390 000–510 000 cases of MDRTB emerged globally [best estimate, 440 000 cases]. [20] Pakistan ranks eighth among the list of 22 high TB burden countries with a TB related death rate of 43/100,000 population annually. [21] The growth of the drugresistant TB epidemic in Pakistan is presented as challenges for the National Tuberculosis treatment Plan [NTP]. In a developing country like Pakistan inpatients treatment for MDR TB is not possible because of low resources and prolonge treatment duration and thus out-patient and Community-based treatment strategies have come into existence. Community-based treatment for drug-resistant TB has successful outcomes and have been reported elsewhere in the world [17]. There have been certain public-private partnerships and non-governmental organizations that has developed community-based treatment projects in parts of Southern Africa. [22,23] The main opinion in favor of in-patient treatment for drug-resistant TB relate to the need to administer and monitor complex, toxic drug regimens and to limit the community spread of drug-resistant TB. However there is no proof that hospitalization actually limits community transmission and it is likely that most patients have been infectious for several months before hospitalization, [12] Moreover, the risk of hospital acquired infection transmission, both to other patients and to health care workers, is also high. [14,15] More importantly there are also economic and social costs involved in keeping patients isolated in hospitals, often away from their residence, and this can lead to default from treatment programs. [16] and therefore there is a salient need to build up community based strategy for the treatment of drug resistant TB patients. [24] In our study as per successful outcome, 110 [72.84%] patients were having successful outcome. [Table No. 6]. These results support the evidence that it is feasible to develop a community based treatment program for the patients who had MDR- TB. The major drawback of this strategy found to be is the high defaulter rate although we could not identify the exact cause of the defaulters was not known but most likely is the lack of education and cost of medications are the major hindrance. If the above two major hurdles are overcome than these MDR-TB patients can be safely managed within the existing infrastructure of the TB program where the expertise is available on an out-patient basis. Regarding the side effects 52.8% developed some side effects due to medications but all are mainly minor in nature, they did not required to discontinue the therapy and are managed accordingly as out-patient. This again favors that hospitalization is not usually necessary for the management of the side effects. [25] One interesting finding of our study is the presence of high resistance pattern of other first line drugs including Pyrazinamide [77.4%], Ethambutol [73.6%], and Streptomycin [69.4%]. This is likely because of the fact that majority of our patient had got secondary MDR TB [90.6%] in which around one third [69.8%] had been treated with antituberculous drugs multiple times which is a risk factor for developing MDR TB.

Management of multidrug-resistant TB [MDR-TB] patients already having psychiatric illnesses such as anxiety and depressive disorders or can develop due to treatment. A mental health assessment before MDR-TB treatment initiation may assist in early diagnosis and better management of psychiatric illnesses in patients already having two stigmatizing and debilitating diseases.[6] A study shows 51 patients [96.2%] had pulmonary while 3 patients [5.6%] had extra-pulmonary TB. History of exposure to tuberculosis patients was found in 36 [67.9%] patients. Treatment regimen with 2nd line drugs was decided on individual basis according to DST on sputum culture results. The mean duration of treatment was 18 months. Successful outcome was seen in 25 patients [47.2%], 25 patients [47.2%] were loss to follow up and defaulted while 3 [5.6%] patients remain smear positive at the end of treatment[7] which as per successful outcome, 110 [72.84%] patients were having successful outcome. [Table No. 6]. Success rate was 89.2% in those who completed the treatment. Treatment of MDR-TB is resource intensive and lasts for 24 months or more, requiring a combination of second-line drugs that are more expensive, less effective and more toxic than those used in standard first-line treatment regimens [8,9] as per successful outcome, 110 [72.84%] patients were having successful outcome. [Table No. 6]. The cure including response rate of MDR-TB without human immunodeficiency virus [HIV] infection using individual tailored regimens was

reported from 39% to 96 % in initially hospitalized patients. [10-14]

CONCLUSION:

This study concludes that out-patient treatment strategy success rate was 72.84% and it is feasible and safe for the treatment of MDR-TB patients.

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