Financial burden of Multi-Drug-Resistant Tuberculosis on patients visiting PMDT sites in Pakistan

ABSTRACT:

Background: One of the main components of END TB strategy is that no families of the patients suffering from any form of Tuberculosis has to suffer from the catastrophic costs. The catastrophic costs can be direct or indirect costs. Keeping this strategy in focus we planned to conduct the economic burden faced by the cases and the households of multi-drug resistant Tuberculosis cases in designated PMDT sites of Pakistan.

Objective: To determine the financial burden faced by the patients of Multi drug resistant (MDR) tuberculosis attending PMDT sites in Pakistan

Methodology: This cross-sectional facility-based study was designed to be implemented in 6 PMDT sites located in all four provincial capitals, federal capital and regional capital providing treatment to the MDR tuberculosis patients. A sample size of 720 was statistically calculated and distributed equally among all the sites with 120 cases of MDR TB to be enrolled from each sites. WHO approved and validated tool translated in local language Urdu was used to calculate the financial burden faced by the MDR TB cases in Pakistan. Direct costs including direct medical cost and direct non-medical cost incurred by the patients both before diagnosis and during treatment were separately calculated.

Results: A total of 720 cases of MDR tuberculosis fulfilling the inclusion criteria were enrolled after obtaining informed consent from them. The patients of MDR TB were facing more than 17% extra costs than their routine expenses. The patients were bearing the direct medical expense of 139 USD and 132USD on non-medical expenses. Majority of cases reported joblessness and social exclusion after contracting MDR tuberculosis. Even after providing social support to the cases of MDR TB cases the patients had reported substantial decrease in household income after contracting MDR tuberculosis.

Conclusion: The study suggests that the government and the donors need to increase the support provided to the patients of MDR tuberculosis. New Artificial embedded technology needs to be added to improve the adherence of drug-resistant tuberculosis regimen.

Introduction:

Patients who are suffering from tuberculosis had to bear huge costs related to illness and disability[1.] These costs are the drivers that create hurdles in treatment adherence among these patients. Furthermore, these cost drivers not only affect the health outcomes of patients but also the health of household contacts living with them and are also responsible for the disease transmission.[2]

Tuberculosis, being the disease of poor badly affects them and result in exponential loss income[3]. While direct payments including out of pocket medical expenses are vital for their well being and are usually done by the patients from their own pocket.[4] Out of pocket payments are the payments that the Tuberculosis patients had to bear at the time even when they are getting treatment from public sector hospitals and dispensaries.[5]. The share of the out-of-pocket payment is a measure of total health expenditures that MDR Tuberculosis patients must bear and when this cost exceeds 40% of their normal expenditure then it is termed as catastrophic cost. [5]

Direct non-medical costs including cost spent on or during travel to the health facilities and purchase of nutritional supplements is also major contributor to the financial burden faced by MDR-TB patients. Since the treatment span for MDR-TB generally lasts two years, these costs have direct impact on the livelihoods of patients. Although in many Governments in LMICs generally provide different types of support schemes to the MDR-TB patients to cope with the economic burden being faced by them during the treatment. They usually provide free of cost medicines, meal vouchers etc. but data suggest that there is lot more to be done. [7-9] In addition to the direct medical and non-medical costs, it is also imperative to measure the indirect loss related to the loss of time from work or loss of job etc. In this situation the affected household generally goes for some coping strategies to overcome or minimize the financial burden faced by them due to MDR tuberculosis [11]. The extent of the financial burden posed by MDR tuberculosis and the coping strategies adopted by the affected household determines the level of hardship.

Worldwide, Pakistan is ranked fifth among countries with high burden of tuberculosis and it accounts for 61% of the TB burden in the WHO Eastern Mediterranean Region. Pakistan has estimated 510,000 new TB cases emerging each year and approximately 15000 among them

developed drug resistant TB. Pakistan has the fourth highest prevalence of multidrug-resistant TB (MDR-TB) globally[1]. Key reasons for emergence of drug resistance TB include delays in diagnosis, unsupervised, inappropriate, and inadequate drug regimens, poor follow-up and lack of a social support program for high-risk populations.

The problem is that MDR tuberculosis patients in developing countries must bear multiple costs including cost incurred on diagnosis, seeking health care, travel, food but also cost for associated disability[2]. Such costs not only create access and adherence barriers but also affect health outcomes and increase the risk of disease transmission. These costs also contribute to the economic burden on households. It is estimated that on an average, a tuberculosis patient of low- and middle-income countries, have to bear the cost which is almost half of his/her annual income[3] Keeping all the facts in line it is therefore recommended as per END TB Strategy, to measure the catastrophic costs, when the total costs exceeds more than 20% of their house hold expenditures. [10]

It's an open truth in science that quality data has pivotal role in formulation of appropriate and effective policies and interventions. Data is also needed to monitor progress toward the End TB Strategy target to eliminate catastrophic total costs due to MDR TB. Keeping in view this study was conducted in Pakistan with an objective to determine the financial burden faced by the patients of Multi drug resistant (MDR) tuberculosis attending PMDT sites in Pakistan

Methods:

Study type, duration and settings: - This facility based descriptive cross-sectional study of one year duration was conducted on 720 patients of Multidrug resistant tuberculosis visiting six PMDT sites for treatment.

Sample Size: By using the estimated cases of MDR-TB as 50000 in Pakistan at 95% CI and 5% margin of error the sample size was found to be 720 cases. The cases were distributed and enrolled equally from all the six PMDT sites.

Inclusion & Exclusion criteria:- MDR tuberculosis patients of both genders and any age group who were either into the intensive or continuation treatment phase for at least two weeks and were reporting in selected PMDT site were included in study, while newly diagnosed patients who had either not started treatment, or those who were on the current treatment phase for less than two weeks were excluded.

Data collection tool and its description: - Data was collected using pretested and validated questionnaire developed by WHO in 2017 for calculation of tuberculosis patient cost. This tool was translated into the local language (Urdu). The survey instrument had four parts. There are 4 following parts of this questionnaire. **Part I:** In this part patient information specific to treatment including date of diagnosis, treatment phase, treatment registration group etc. were obtained from TB treatment card before interview (This part will be filled from all eligible patients), **Part II:** This part primarily comprises Consent form (This part was filled for all eligible patients)**Part III:** Costs before the current MDR -TB treatment. In this section following information were collected Out-of-pocket expenditure, reimbursements and time loss for the diagnosis and before start of TB treatment will be calculated in this part**.** (This part was filled only for new cases in the intensive phase only) Part **IV:** Cost during current MDR-TB treatment. The information gathered in this part of the questionnaire included cost during outpatient visits for medical follow-up, costs for nutritional/food supplements, time loss, ssocial position, income (reported) before contracting TB, Income changes and social consequences, coping strategies (information for this part was collected from all enrolled patients)

Estimation of past and future costs during the entire illness episode was possible from the data collected from MDR TB patients either in intensive or continuation phase. As no follow-up interview was needed, data collection could be completed in one year.

Direct cost was calculated from the cost paid by patients while seeking or accessing MDR-TB services and it includes both medical and non-medical payments, net of reimbursements. Direct medical costs incurred before diagnosis, during treatment or hospitalization, cost on medical visit for checkup to just to collect MDRTB drugs. For hospitalized patients' further costs were subcategorized in bed day charges, consultation fees, radiography, medicines, laboratory tests, and other procedures if the respondent can disaggregate them. Direct non-medical costs included the cost of transportation to and from a medical visit and the cost of food that the patient (and their accompanying household members) had to purchase while travelling to a health facility. This also included food needed during hospitalization or nutritional supplements or special food recommended apart from regular food by the consultant or treating physician. Sometimes patients had to travel for more than one day to seek care and, in this instance, the cost of overnight accommodation was also included as a direct non-medical cost. In cases when patients and their caregivers were relocated to another town or city treatment of MDR tuberculosis in that situation cost incurred on relocation and new accommodation was also considered as direct non-medical cost.

Indirect cost was calculated through the income that patients or their caregiver reported as lost during treatment, or through a measure of the opportunity cost for seeking or being in care, that is a valuation of time "lost" for the patient and their household members throughout the TB episode. This study collected that allowed the estimation of indirect costs through two alternative methods: the output approach and the human capital approach. The output approach used self-reported household income at three points in time (prior to the onset of TB symptoms, at the time of diagnosis and during the "current" treatment phase) to estimate income change before and during the TB episode.

Procedure:

Ethical approval was taken from National Bioethics Committee of Pakistan. Health departments of all four provinces, federal capital and AJK were contacted to obtain their consent and permission for participation in the study. Once appointment given, Investigators visited them to brief about project objectives and methodology. In the same meetings PMDT sites from each

province, federal capital and AJK were selected after detailed discussion with relevant stakeholders and authorities. Urdu version of the tool was pilot tested on 43 patients i.e. 6% sample size. Each selected PMDT site filled 07 questionnaires from patients fulfilling the inclusion criteria. Filled questionnaires were shared with investigators who checked questionnaires for clarity and based on findings translation of some questionnaires was revised to ensure that essence of each question is well translated and easily understandable both for interviewer and interviewee. To maintain uniformity in data collection process an operation manual for the interviewers was developed by the investigators. Investigators visited each of the selected PMDT sites for coordination meetings with their respective heads to brief them about overall project objectives and methodology along with timelines.

At each of the six PMDT site a 03-member team comprising one male, one female interviewer and a supervisor was formulated. Each team was trained in the sampling strategy, how to take consent, enrollment process, proper administration and filling in the questionnaires along with explanation of each question on the questionnaire. Data collection process has started simultaneously at all six sites.

MDR-TB patients monthly visit the sites for follow up and some are admitted. Therefore, patients were enrolled both from outpatient department and admitted ones. The interviewer briefly explained the study objectives to the patients fulfilling the inclusion criteria. The patients were informed that interview may take his/her 15 minutes. Time is given to literate patients to read and understand the consent form translated in national languages Urdu. Consenting patients were taken to a separate cabin/room allocated for interviews to ensure patients privacy and confidentiality along with infection control. Interviewer collects data on pre- tested and validated questionnaire. Post interview, the interviewer completes some questions by checking patient records, which also took approximately 15 minutes. Data was entered and analyzed using SPSS version 21.

Results:

In this study a total of 720 cases of multi-drug-resistant tuberculosis were enrolled. Regarding the socio demographic variables of the enrolled patients, it was found that majority of the cases, 313 (44%) were illiterate and only 12 (1.7%) patients were graduates. Amongst enrolled cases 385(53.5%) were males and 335(46.5%) were females. (Table1)

Table 1: Socio demographic variables on enrolled MDR Tuberculosis patients

Variables		Number (n)	Percentage (%)
Sex	Male	385	53.5%
	Female	335	46.5%
Education	Illiterates	313	44%
	Primary School	161	22%
	Secondary School	177	25.0%
	University	35	4.9%
	Graduate School	12	1.7%
	Other	22	3.0%

Further 671(96%) cases of the MDR TB were of pulmonary TB while only 29 cases were of extra pulmonary origin. Around 566 (79%) cases were diagnosed at public sector health facility. Nearly 433 (60.4%) cases were new cases of MDR TB. Only 18 (2.8%) cases were currently hospitalized.

Furthermore, majority of the enrolled cases of MDR TB had not basic amenities like washroom 210(29.8%), while (321)44.5% were using pipe water and 283(40%) were using some other sources of drinking water. The details are given in table-2

Table 2: distribution of Socioeconomic variables among enrolled MDR TB patients (n=720)

Variable		Number (n)	Percentage (%)
Source of Drinking Water	Well	116	15.6%
	Pipe or bottled	321	44.5%
	Other	283	39.9%
Toilet Facilities	Flush Toilet	495	70.2%
	Other	215	29.8%
Household Have Electricity	Yes	602	85.0%
	No	108	15.0%

Households Have TV	Yes	487	68.8%
	No	233	31.2%
Household Have Motorcycle	Yes	368	58.9%
	No	257	41.1%
Household Have Wardrobe	Yes	145	26.2%
	No	409	73.8%
CD/DVD	Yes	37	6.7%
	No	519	93.3%

Before getting diagnosed as sufferer of MDR tuberculosis, Pakistani patients had to bear huge cost for many expenses. These include direct medical costs for laboratory and radiological testing etc. Mean of the aggregated medical cost is 124.26 $\pm$ 124 USD, while non-medical cost is 46 $\pm$ 96 USD. Overall total out of pocket cost to be paid is 93 $\pm$ 132 USD. (Table 3)

Table 3: Cost incurred by MDR tuberculosis patients of Pakistan before treatment initiation in 2021 (USD)

		Mean	Standard Deviation	Minimum	Maximum
Time spent (Hours)	Total Duration (Hours)	6.74	3.69	0.12	24.00
	Hospitalization Visits	7	6	1	22
	Travel time (Hours	3.73	2.91	.25	12.00
	Time spent on visiting (Hours)	2.30	1.77	.25	13.00
	Day Charges	56	93.1	3.22	400
Medical Cost (US$ Dollars)	Consultation Fee	7.21	9.22	1.5	63.3
	Radiography and Imaging	30.5	56.34	3.5	400
	Lab Test	42.06	74.84	3.5	533.33
	Other Procedures	32.8	38.65	1.8	133.3
	Medicines	39.22	82.32	0.7	566.
	A= Aggregate Medical Cost	124.26	124.8	3.5	1020
Non-Medical Cost (US$ Dollars)	Travel	7.23	9.24	0.3	66.66
	Food	3.74	11.66	0.3	166.66

	Accommodation	9.33	5.42	0.8	13.33
	Supplements	6.66	14.47	0.8	106.6
	B= Aggregate Non-Medical Cost	46	96.03	0.8	1144
Total Out of Pockets	Payments(A+B)	93.67	132.44	0.8	1144
	Health Insurance reimbursement	0	0	0	0
Net out of pocket Payments	(A+B+C)	93.67	132.44	0.8	1144

After being diagnosed at the PMDT site for the treatment initiation, the patients still undergone huge expense in terms of direct medical and indirect medical costs. For the direct medical costs, the patients are still bearing the cost of 139 USD after being diagnosed and treated free of cost at the PMDT sites. Furthermore, an estimated 132USD is being spent by each MDR TB cases as a non-medical expense. In total the cases of MDR TB had to bear the cost of 271 USD in addition to their routine expenses. (Table 4)

Table 4: Cost incurred by MDR tuberculosis patients of Pakistan during treatment at PMDT sites in 2021 (USD)

		Mean	Standard Deviation	Minimum	Maximum
Medical	Hospitalization Visits	1	0	1	3
	Total Number of days (sum of all cells in Table)	17.84	22.65	.25	90.00
	Travel Time (Hour)	4	3	1	12
Medical Cost (US$ Dollars)	Consulation_MedicalQ23	17.33	25.47	4	93.3
	Radiography and ImagingQ23	3624	31.55	300	21000
	Lab TestQ23	32.96	52.66	1.5	300
	Other ProceduresQ23	40.16	113.4	0.1	566.6
	MedicinesQ23	31.10	63	1.1	433
	Supplements and OthersQ23	18.32	28.63	0.8	133
	A= Aggregate Medical Cost	139.18	232.63	2.33	1746.4

Non-Medical (US$ Dollars)	TravelQ23	8.75	10.65	0.45	40
	FoodQ23	16.4	29.14	0.45	166.66
	OthersQ23	5.1	6.30	0.45	33.33
	B= Aggregate Non-Medical Cost	27.5	35.37	0.45	200
Total Out of Pocket Payments	Payments(A+B)	132.10	221.3	0.45	1778
	C= Health Insurance Reimbursement	.	.	.	.
Net Out of Pocket Payments	A+B+C	132.10	221.31	1.45	1778

There is change in the income of households before diagnosis of MDR Tuberculosis, after diagnosis and at time of interview. On an average net household income is decreased from 245 USD to 205 USD in Pakistani MDR TB patients. (Table 5)

Table 5: Pattern of Household annual income among MDR Tuberculosis patients on Pakistan in 2021 USD (n=720)

	Mean	Standard Deviation	Minimum	Maximum
Net Household Income Before MDR Tuberculosis (US$ Dollars)	245.72	195.42	13.3	2333
Net Household Income at the time of Diagnosis of MDR Tuberculosis (US$ Dollars)	201.5	137.44	13.3	1666
Net Household Income after MDR Tuberculosis (US$ Dollars)	205.64	235.15	6.66	2666.6
Working Days of Income Lost due to MDR Tuberculosis (US$ Dollars)	64.8	122.9	1.0	900.0

MDR Tuberculosis affected patients experienced bad impacts both on their social life and financial situation. Around 110(15%) patients experienced social exclusion while food insecurity was experienced by 92(12.8%) patients. Further 447 (68.3%) patients believed they became poorer after encountering MDR Tuberculosis. (Table 6)

Table 6: Impact of MDR Tuberculosis on social life and financial status of patients

		Frequency (n)	Percentage (%)	95.0% Lower CL for Column N %	95.0% Upper CL for Column N %
Effects of MDR - TB illness on social and private life of patients	None	200	27.8%	24.6%	31.1%
	Food Insecurity	92	12.8%	10.5%	15.4%
	Divorced and separated	2	0.3%	0.1%	0.9%
	Loss of Job	38	5.3%	3.8%	7.1%
	Interrupted schooling	21	2.9%	1.9%	4.3%
	Social Exclusion	110	15.3%	12.8%	18.0%
	Multiple among above all	257	35.7%	32.3%	39.2%
Impact on financial situation of the household after MDR TB	Richer	4	0.6%	0.2%	1.4%
	Unchanged	181	27.7%	24.4%	31.2%
	Poorer	447	68.3%	64.7%	71.8%
	Much Poorer	22	3.4%	2.2%	5.0%

Patients of MDR tuberculosis adopted different coping mechanisms and around 280(40%) patients borrowed amount more commonly from family members 98 (13.6%). Around 199 (37.8%) patients sold their property to compensate financial losses. (Table 7)

Table 7: Coping mechanisms adopted by MDR Tuberculosis patients

Coping mechanisms		Frequency (n)	Percentage (%)	95.0% Lower CL for Column N %	95.0% Upper CL for Column N %
Borrow or received any money to Cover the TB Treatment	Yes	280	40.4%	36.8%	44.1%
	No	413	59.6%	55.9%	63.2%
Whom you Borrowed that Money	Family	98	13.6%	11.3%	16.3%
	Neighbors	70	9.7%	7.7%	12.0%
	Private Bank	36	5.0%	3.6%	6.8%
	Cooperatives	0	0.0%	.	.
	Employer	11	1.5%	0.8%	2.6%
	Unofficial Lander/ Black Market	3	0.4%	0.1%	1.1%

	Others	24	3.3%	2.2%	4.8%
	Multiple sources	478	66.4%	62.9%	69.8%
Are you expected to pay the amount back	Yes	259	72.1%	67.3%	76.6%
	No	21	27.9%	23.4%	32.7%
Have you sold any of your property to finance TB Treatment	Yes	199	37.7%	33.6%	41.9%
	No	329	62.3%	58.1%	66.4%
What did you Sell	Land	18	2.5%	1.5%	3.8%
	Livestock	113	15.7%	13.2%	18.5%
	Vehicle	11	1.5%	0.8%	2.6%
	Household Items	5	0.7%	0.3%	1.5%
	Jewelry	35	4.9%	3.5%	6.6%
	Other	16	2.2%	1.3%	3.5%
	Multiple	522	72.5%	69.2%	75.7%

Discussion:

Despite the availability of free medicines and meal vouchers and social support given to the cases of the MDR TB in Pakistan, it is very much clear that the patients and their households are facing huge financial burden due to either loss to their incomes, exclusion from the society etc. In our study the economic burden is assessed by more than 17% of the cases of MDR-TB which is not in line with the study reporting the ratio of 35%[12].

In our study the direct medical costs expenditures of the MDR-TB cases account for 139USD on medical and 132USD non-medical expenses. The values given are not in line with the study reported the value of 130USD for medical expenditure and 265 for non-medical expenditure[12,] Another study from three different countries had reported the ratio of about 260USD in Ethopia,169USD in Indonesia and 929 for kazakhustan.[9]One of the main drivers in the direct non-medical spending by the cases of MDR TB are the supplements and the food items they have to purchase from their own pocket. Another study had reported the same information that food and other essential items were the main cost addition factors[9]. In terms of the direct medical cost the main driver behind the costing is the additional medicines that the cases purchase other than those provided free of cost to the cases of TB. Our study confirms the previous studies which state that the MDR TB cases had to face more financial burden because of the longer duration of MDR TB [13-14].

Although this study was done in 6 different PMDT sites but it has a limitation that it was mainly conducted on the patients who were visiting the sites who are working under national TB control program of Pakistan. The study does not involve cases from the private sectors. So, this results in exclusions of cases who do not seek care altogether or those who rely mainly in the private sector. Furthermore, the COVID-19 pandemic has also led to the decreased enrollment of cases and financial impact varied massively on the TB cases. Despite the availability of the private sector, patients rely mainly on the public health services for their enrollment and decreased cost as compared to the private facilities.

One of the main issues of the study was recall bias in the cases who were enrolled in the DR-TB control program. We tried to minimize the bias from our study by asking about current treatment mainly and previous expenditures were asked only to form the intensive phase cases only. From the continuation phase cases the cost the patient bears are only available for that time, and the situation may change invariably, and the cost may exceed drastically then the calculated ones.

Despite the data available the indirect costs of MDR TB case may increase in variably for those cases who are declared as cured. Effects of the coping strategies like selling essential items, removal of children from school also need to be evaluated and they impact he household massively for years [12]. To combat the costs of travel, food, medicines the government of Pakistan with the support of external partners are supporting the cases with either meal vouchers, travel costs, free medicines etc. This results in the enrollment of the MDR-TB cases more in the

public sector programs than in the private sectors. Furthermore, the global fund is also supporting the MDR-TB cases in variably and providing support to the patients and households in Pakistan.

In the summary this study has clearly showed the costs faced by the MDR-TB cases in Pakistan and where interventions need to be done and strengthen to eliminate the TB menace.

Institutional Review Board: ERB was taken from national Bio-ethics committee of Pakistan.

Informed Consent: Informed consent was taken from all enrolled cases.

Conflict of interest: The author declares no conflict of interest.

Acknowledgment: - We hereby acknowledge WHO, EMRO regional office for providing funding for this study through Joint EMRO/TDR Small Grants Scheme for Implementation Research in Communicable Diseases 2020-2021. Scientific referral number for this grant was SG-20-42.

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