Depression and its Associated Factors with Multidrug-Resistant Tuberculosis at Baseline

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Abstract

Background: Both depression and Multi-drug resistant tuberculosis (MDR-TB) are global public health problems with substantial impact on human health. However, depressive state among MDR-TB patients has not been well investigated in Pakistan.

Objective: To assess frequency of depression and to identify factors associated with depression at baseline among MDR-TB patients in our centre.

Method and design: This was a cross sectional study conducted at programmatic management of drug resistant TB unit (PMDT), Lady Reading Hospital Peshawar (LRH), Pakistan. A total of 289 MDR-TB patients were included in the study, which were enrolled for treatment in this unit from January 2012 till December 2013 and assessed at the time of registration for depression. Convenient sampling technique was used for data collection.

Result: A total of 289 patients were included in this study. Among total, 201(69.55%) of the study participants were classified depressed, 127 patients (63.18%) had mild depression, 61 patients (30.35%) had moderate depression, 13 patients (6.46%) were diagnosed with severe depression. Depression was found in 127 (43.9%) MDR-TB patients at the time of registration associated with different factors.

Conclusion: Gender, duration of illness, residence, co-morbidity and past TB treatment were associated and independent risk factors of depression.

Keywords: Depression; MDR-TB; PMDT; SLDs; Peshawar; Pakistan

Introduction

The emergence of drugs resistance and in particular multidrug-resistant tuberculosis (MDR-TB), defined as resistance to isoniazid (INH) and rifampicin (RIF), has posed serious challenges in controlling TB [1,2]. Compared to first-line anti TB therapy, compliance with MDR-TB treatment is considerably difficult because of its prolonged duration and frequent adverse effects of second-line drugs (SLDs) [3].

Psychiatric complications are commonly associated with MDRTB both at baseline and due to SLD's use. Baseline depression in MDRTB patients before the treatment is started was found in 65% patients in a study in Pakistan.4 According to the findings of another study from Lima, Peru baseline depression was observed in 52.2% in MDR-TB patients. Reason stated for baseline depression in patients with MDR-TB include fear and guilt associated with infectious risk; the socio-economic and psychological burdens of living with a chronic, life-threatening illness; increased dependence on others; multiple treatment failures and being told in health centers that no further therapy was available; losing family members to the disease; and concomitant poverty [4]. Social stigma, which may produce social isolation, diminished marriage prospects, limited social support, and may result in the denial of diagnosis and consequent rejection of treatment [5].

The frequency of psychiatric disorders associated with MDR-TB treatment has been reported to be 21.3% patients [6], 22% of MDR-TB patients [7,8]. Reported rate of depression in MDR-TB varies from 6.2% to 22% [3,9-11]. Several authors have described how these psychosocial factors complicate adherence to drug regimens, and emphasize the importance of attention to mental health in order to ensure positive treatment outcomes [5].

Although most commonly psychiatric complications have been associated with INH, ethionamide (ETO), ethambutol (EMB) and

fluoroquinolones are also known to cause such complications. Severe psychiatric manifestations including hallucinations, anxiety, depression, behavioral disorders, and suicidal ideation and/or attempts have been reported to occur in 9.7% to 50% of individuals receiving anti TB drugs [12,13]. Several case reports associate the use of ETO with occurrence of depression, anxiety, psychosis, and suicide [3].

While adverse effects associated with MDR-TB therapy may be controlled effectively, some of these need special attention [14,15]. Psychiatric problems such as depression can significantly affect patient quality of life, as well as physician's approach toward MDR-TB therapy. Consequently, effective management of depression is critical not only for desired patient outcome, but also for patient's overall health and physician's satisfaction while dealing with MDR-TB therapy [16].

Depression may also adversely affect the compliance to treatment and result in default which in turn may have serious consequences of treatment failure and further extension in drug resistance. Depression may be a very important negative factor to treatment adherence for patients on tuberculosis treatment [17,18]. Despite the fact that Pakistan is among high prevalence country for MDR-TB, there is little

data available about depression among MDR-TB patients, it providing us justification for this study.

All PMDT sites in Pakistan have a psychologist to address the issue of frequent psychiatric complications associated with MDR-TB treatment. That's why in spite of the side effects the reported treatment success rate of MDR-TB patients is 78.7% in Pakistan [19].

This topic is of great importance but there have been very few studies done so far to assess the frequency of depression at the time of registration for MDR-TB treatment and its associated factors. So this study is proposed to find it which is very important component for the successful treatment of MDR-TB.

Methods

Study design

This was a cross sectional study conducted to describe frequency of depression and other associated factors among MDR-TB patients at baseline (at the time of registration for MDR-TB treatment).

Subjects

A total of 289 MDR-TB patients were included in the study, which were enrolled for treatment in this unit from January 2012 till December 2013. Convenient sampling technique was used for data collection.

Data collection

Patient interviews were conducted by one data collector using a structured questionnaire. The structured questionnaire was designed to assess socio-demographic factors such as marital status, socio-economic status, age, gender, duration of past treatment; weight, monthly income, residence, co-morbidity and patients contact status. All registered MDR-TB patients were assessed individually. After developing rapport with each patient, Psychological assessment was performed by a clinical psychologist using diagnostic and statistical manual of mental disorders, fourth edition (DSM-IV TR) criteria for depression and Hamilton Depression Rating scale. Every patient was assessed at the time of registration.

Tools

Hamilton Depression Rating Scale subsequent: Hamilton depression rating scale (HAM-D) was used to assess depression among MDR-TB patients. The HAM-D scale consists of 20 questions according to the criteria of major depression as per the diagnostic and statistical manual of mental disorders, Fourth Edition, Text Revision (DSM-IV-TR). Total score range from 0 to 57 and indicate the severity of depression. In addition, the scoring is based on the first 17. It generally takes 15-20 minutes to complete the interview and score the results. It's a valid and reliable scale. Test-Retest reliability for Hamilton depression scale ranged from 0.65 to 0.98 according to a meta-analysis over a period of 49 years [20] whereas according to our study .84 is the reliability of this scale.

Ethical approval

The study was approved by Research and Ethics Committee of the Postgraduate Medical Institute, Peshawar, Pakistan.

Statistical analysis

Following are the risk factors analysed for association with depression: sex, age, and marital status, positive history of past TB treatment and occurrence of any co-morbidity. Multivariable analysis

was carried out using multiple regression model inclusive of all variables associated with a P value ≤ 0.05 or an odds ratio (OR) > 2.0 on univariate analysis.

Reported P values were based on two-sided Fishers exact tests, or for continuous variables, t-tests or, if non-parametric, the Wilcoxon test. For binary variables, ORs with 95% confidence intervals (95% CIs) were also calculated. For this purpose, statistical package for social sciences version 20 were used.

Results

Total number of 289 patients was included in this study. Baseline characteristics of patients treated in the 2012 at this centre are described in Table 1. These patients were from different district of Khyber Pakhtunkhwa, FATA and Afghanistan, but maximum numbers of the patients (33%) were from district Peshawar, and a hundred and sixty-three (56.0%) cases were from rural areas. Mean age of the study cases was 29.88 years ranging from 10 to 70 years; 53.6% were female. Sixty percent of patients (60.2%) at the time of their treatment were married. Baseline weight of maximum number of patients was between 40-60 kg ranging from 16-78 kg with an average of 44 kg. Co-morbidity was found in Eighty-five (29.4%) patients. Most of the study cases (61.2%) were of lower socio economic status with monthly income lower than ten thousand rupees monthly.

Depression was not found in 88(30.45%) patients, whereas 201(69.55%) of the study participants were classified as depressive on the HAM-D scale, 127 patients (63.18%) had mild depression, 61 patients (30.35%) had moderate depression, 13 patients (6.46%) were diagnosed with severe depression. The prevalence of depression was assessed in each group, as well (Table 2). Depression was found in 127 (43.9%) patients at the time of registration for MDR-TB treatment.

Factors associated with depression

Univariate analysis (Table 3) showed that patient with female sex (p = 0.003), younger age (≤ 30 years vs >30 years) (p = 0.028), residence of urban area (p=0.05), longer duration of sickness (p<0.001), previous use of second line tuberculosis drugs (SLDs) (p = 0.05), any co-morbidity (p = 0.001), poor socioeconomic status of the family (p = 0.016) and poor outcome of previous TB treatment (p<0.001) were associated with depressive state.

In a multivariate regression model, longer duration of illness (OR 0.156, 0.061-0.398, p<0.001), residence of patient (OR 0.302, 0.116-0.781, p=0.014), and poor outcome of their past TB treatment (OR 0.109, 0.042-0.285, p < 0.021) were independent risk factors of depressive state of MDRTB patients during their treatment. This analysis showed that depression is found three times more in female patients as compared to male patients (OR 3.147, 1.189-8.329, p=0.021). Presence of any other co-morbidity increased the risk ten-fold (OR 10.521, 2.459-45.010, p=0.002) (Table 4). This model fit was based on nonsignificant Hosmer and Lemeshow test (p=0.803) and overall percentage of 87.2% from classification table.

Discussion

Multi drug-resistant TB offers a great challenge to TB control programs. Psychiatric complications are commonly associated with MDRTB. Both depression and Multi-drug resistant tuberculosis (MDR-TB) are global public health problems with substantial impact on human health. However, depression and its associated factors among MDR-TB patients of great importance but there have been very few

Patients characteristics	No. of patients (%) N = 289	Median (range)
Demographics		
Gender		
Male	134 (46.4)	
Female	155 (53.6)	
Age (Years)		29.88 (10-79)
10-14	14 (4.8)	
15-19	58 (20.1)	
20-24	62 (21.5)	
25-30	49 (17.0)	
31-34	22 (7.6)	
35-39	16 (5.5)	
40-44	20 (6.9)	
45-49	15 (5.2)	
≥50	33 (11.4)	
Weight (Kg)		44.87 (16-78)
<40	91 (31.5)	
40-60	183 (63.3)	
>60	15 (5.2)	
Monthly Income		
Rs. ≤ 10,000	177 (61.2)	
Rs. 11 – 20,000	97 (33.6)	
Rs. > 20,000	15 (5.2)	
Residence		
Urban	126 (44.0)	
Rural	163 (56.0)	
Marital Status		
Married	174 (60.2)	
Unmarried	114 (39.4)	
Widow	1(0.3)	
Co-Morbidity		
Yes	96 (33.)	
No	193 (66.8)	
Patients contact status		
No Contact	208 (72.0)	
Drug-susceptible TB	45 (15.6)	
Drug-resistant TB	36 (12.4)	
Previous TB treatment		
Yes	262 (90.65)	
No	27 (9.35)	
Duration of TB disease (years)		3 (2-7.6 yrs)
Previous TB treatment episodes		3 (1-5 Episodes)
Less than or equal to 1 year	58 (20.1)	
Greater than 1 year	231 (79.9)	
Previous use of second-line drug		
Yes	24 (8.3)	
No	265 (91.7)	
Previous TB Treatment Category		
CAT I	151 (52.2)	
CAT II	138 (47.8)	
Previous TB Treatment Outcome		
Successful treatment outcome	46 (15.9)	
Unsuccessful treatment outcome	243 (84.1)	

Table 1: Baseline characteristics of study cases.

Variables		Depression	
		Yes	No
Gender	Male	109 (81.3)	25 (18.7)
	Female	144 (92.9)	11 (7.1)
Age	10-14	13 (92.9)	1 (7.1)
	15-19	54 (93.1)	4 (6.9)
	20-24	54 (87.1)	8 (12.9)
	25-29	45 (91.8)	4 (8.2)
	30-34	19 (86.4)	3 (13.6)
	35-39	10 (62.5)	6 (37.5)
	40-44	18 (90.0)	2 (10.0)
	45-49	12 (80.0)	3 (20.0)
	≥50	28 (84.8)	5 (15.2)
Weight	<40	84 (92.3)	7 (7.7)
	40-60	153 (85.0)	27 (15.0)
	>60	16 (88.9)	2 (11.1)
Residence	Rural	105 (83.3)	21 (16.7)
	Urban	148 (90.8)	15 (9.7)
Marital Status	Unmarried	101 (88.6)	13 (11.4)
	Married	151 (86.78)	23 (13.22)
	Widow	1 (100)	0
Previous TB treatment episodes	≤ 1 year	37 (63.8)	21 (36.2)
	> 1 year	216 (93.5)	15 (6.5)
Co-morbidity	Yes	93 (96.9)	3 (3.1)
	No	160 (82.9)	33 (17.1)
Monthly income (Rs.)	≤ Rs. 10 thousand	160 (90.4)	17 (9.6)
	Rs. 11-20 thousand	79 (81.4)	18 (18.6)
	> Rs. 20 thousand	14 (93.3)	1 (6.7)
Past TB treatment outcome	Successful treatment outcome	26 (56.5)	20 (43.5)
	Unsuccessful treatment outcome	227 (93.4)	16 (6.6)
Previous use of SLD	Yes	24 (100)	0 (0)
	No	229 (86.4)	36 (13.6)

Table 2: Association of depression with other factors.

studies done so far to assess the depression at the time of registration for MDR-TB treatment and its associated factors. So this study is proposed to find this very important component for the successful treatment of MDR-TB.

There is growing interest in psychiatric co-morbidities in population with physical illness and understandings to its unwanted consequences particularly poor adherence [21]. Primary aim of this study was to find out the rate of depression and factors responsible for it among MDR-TB patients. Frequency of depression observed in this study (87.5%) was much greater as compared with the prevalence in the general population of Pakistan (45.98%) [22]. This study finding is much greater as compared with 11% found by Aghanwa and colleague in Nigeria [23], 19% found in Turkey [24], 49% found by Natani and colleagues in India [25] and comparable with 80% found in hospitalized patients in Pakistan [26]. Compared with the previous reports in other countries, prevalence of depressive state among MDR-TB patients was relatively higher in the present study. A possible explanation justifying this result may include that MDR-TB treatment is of longer duration with extensive side effects as compared to first line drugs used for drug susceptible TB.

Different studies have identified variety of factors associated with high rate of depressive state in MDR-TB patients including malnourishment, marital status of cohabiting, adverse effects of drugs,

social disgrace, and the physiologic brunt of chronic illness [17], inadequate social support [27].

The present study showed that female patients (p<0.01), younger age (≤ 30 years vs >30 years) (p<0.05), locality of urban areas (p<0.05), longer duration of sickness (p<0.001), previous use of SLDs (p<0.05), any associated co-morbidity (p<0.001), poor socio-economic status of family (p<0.01) and poor outcome of previous TB treatment (p<0.001) were associated with depressive state.

Patients characteristics	Depression		95% CI	Odd Ratio	P-value
	Found	Not Found			
Demographics					
Gender					
Male	109 (81.3)	25 (18.7)	0.157-0.706	0.334	0.003
Female	144 (92.9)	11 (7.1)			
Age (Years)					
< 30	167 (90.8)	17 (9.2)	1.073-4.389	2.170	0.028
≥ 30	86 (81.9)	19 (18.1)			
Weight (Kg)					
< 40	83 (92.2)	7 (7.8)	0.851-4.809	2.023	0.105
≥ 40	170 (85.4)	29 (14.6)			
Marital Status					
Unmarried	101 (88.6)	13 (11.4)	0.569-2.428	1.176	0.662
Married	152 (86.9)	23 (13.1)			
Residence					
Rural	105 (83.3)	21 (16.7)	0.250-1.029	0.507	0.05
Urban	148 (90.8)	15 (9.2)			
Monthly Income					
≤ Rs. 10 thousand	171 (91.0)	17 (9.0)	1.151-4.718	2.331	0.016
>Rs. 10 thousand	82 (81.2)	19 (18.8)			
Co-Morbidity					
Yes	93 (96.9)	3 (3.1)	1.908-21.425	6.394	0.001
No	160 (82.9)	33 (17.1)			
Duration of Sickness					
≤ 1 year	37 (63.8)	21(36.2)	0.058-0.259	0.122	< 0.001
> 1 year	216 (93.5)	15 (6.5)			
Previous use of second-line drug					
Yes	24 (100)	0 (0)	1.103-1.214	1.157	0.05
No	229 (86.4)	36 (13.6)			
Previous TB Treatment outcome					
Successful outcome	26 (56.5)	20 (43.5)	0.042-0.198	0.092	< 0.001
Unsuccessful outcome	227 (93.4)	16 (6.6)			

Table 3: Univariate analysis of factors potentially contributing depressed state (N=289).

Variables	B	S.E.	Wald	df	Sig.	Exp (B)	95 % CI	
							Lower	Upper
Gender	1.146	0.497	5.328	1	0.021	3.147	1.189	8.329
Duration of Illness	1.857	0.477	15.169	1	< 0.000	0.156	0.061	0.398
Residence	1.199	0.486	6.090	1	0.014	0.302	0.116	0.781
Co morbidity	2.353	0.742	10.071	1	0.002	10.521	2.459	45.010
Past TB treatment outcome	2.216	0.490	20.438	1	< 0.000	0.109	0.042	0.285

Note: Only those predictors given in Table which are significant in analysis.
B: Bet, SE: Standard Error, df: Degree of freedom, Exp (B): OR, CI: confidence interval.

Table 4: Multivariate analysis showing factors related with depressed state of MDR-TB patients (N=289).

Women are reported to have high prevalence, incidence and morbidity associated with depressive disorders. Our findings are consistent with other studies where women had higher level of depression than men, also observed by a study conducted in Pakistan [8]. The gender difference is likely to be due to a complex interaction between biological, psychological and socio-cultural vulnerabilities [28]. Female patients with MDR-TB in developing countries become lonely, underestimated and socially stigmatized with consequent depression [29]. Gender depression is also associated with younger age [26]. In the present study all MDR-TB patient with age lower than 30 years, had experienced more episode of depression as compared to older age patients. Possible explanation for the stated reason is that as MDR-TB treatment is for longer duration, expensive, large number of drugs accompanied by wide variety of side effects, thus making young people more prone to loss in their self-esteem and courage [30]. Low maturity level cannot withstand such harsh situation of disease burden as well as social stigma hence leading towards significant depression as compared to old age [31].

An additional significant finding of the current study was positive association of depression with duration of sickness. Patients with longer period of illness experienced higher degree of depression. Reason may include hopelessness, sense of worthlessness, hospitalization, social stigmatization and loss of earning all these factors lead to self-depreciation, conscious and unconscious fear of ailment and death [32,33]. Our study showed positive relation of depression with past treatment outcome and previous use of SLDs. Patients with unsuccessful outcome of past treatment suffer from more depression because of uncertainty of the outcome of the therapy, repeating the same medicines or further additions in therapy, use of SLDs and its known and already experienced side effects [34].

Although in Pakistan the treatment of drug susceptible and drug resistant TB is free of cost [35], the burden of poverty and its psychological consequences, in association with the stigma of MDR-TB, and its physical impact is likely to compound the stress leading to further deterioration of coping mechanisms. MDR-TB patients are physically as well as mentally compromised to be able to lead a productive life, so their socio-economics tend to deteriorate. Consequently, they are unable to support their family resulting in loss of self-esteem, and development of depressive disorders [35].

Depression is also associated with poor adherence to medication, and may be related to medication adherence in MDR-TB patients, although we could not assess the relationship in this study. Screening and follow-up for depression are recommended for MDR-TB patients, which could reduce the disease burden by increasing treatment adherence [17].

Baseline as well as ongoing monitoring of patient's mental health status is very important as it may facilitate the health care professionals, patients and their family members in proper management of a patient's condition during entire illness.

Psychiatric co-morbidities are frequently associated with MDR-TB and their presence is not a contra-indication to MDR-TB treatment, as described by Vega et al. [6]. Care should be individually tailored to help patients cope with the combined burden of depressive symptoms in addition to their illness of MDR-TB.

Conclusion

Depression during MDR-TB treatment needs particular attention. Health care professionals involved in management of MDR-TB patients

should be properly skilled to execute proper mental health assessment tools, in particular at baseline, so that presence of depression can be identified on earlier basis. It is recommended to regularly monitor the mental health status of MDR-TB patients by skilled Clinical Psychologist/counselors, using simple, validated and cost-effective tools.

Strengths

- Highest no of MDR-TB patients come to this PMDT unit for treatment.

- It includes patients from wider geographical areas of KPK, so the results can be generalized to whole of this region.

- All registered MDR-TB patients were included in the study of a well-established and organized PMDT unit of the province.

Limitations

Although this research study was carefully prepared, still the study possesses some limitations.

- The data were collected from only one PMDT unit of Khyber Pukhtunkhwa, Peshawar, Pakistan.

- More studies from other centres would help to understand the problem in greater detail.

- Only depression and its factors were assessed as a psychological problem related to MDR-TB patients while other psychiatric problems were not assessed.

- Depression was assessed only at the baseline.

- Suggestions and Recommendations.

- The data should be collected from all the PMDT units in Pakistan.

- All the psychiatric issues related to different factors of MDR-TB patients should be included in further studies.

- More studies are required to assess the development and progress of depression during the course MDR-TB treatment.

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Author Contributions

Conceived and designed the experiment: SM, Performed the experiments: SM MAK, Data collection: SM NA, Data entry: MAK SM, Analyzed the data: SM MAK, Management of patients: AJ AB MAK SM AK, Wrote the paper: SM MAK and AJ. Revised the manuscript: AJ AB SM MAK MI IU.

References

1. Cole ST (2001) Drug resistance and tuberculosis chemotherapy-From concept to genomics. Bacterial Resistance to Antimicrobials 355.

2. Chiang CY, Centis R, Migliori GB (2010) Drug-resistant tuberculosis: Past, present, future. Respirology 15: 413-432.

3. Vega P, Sweetland A, Acha J, Castillo H, Guerra D, et al. (2004) Psychiatric issues in the management of patients with multidrug-resistant tuberculosis. Int J Tuberc Lung Dis 8: 749-59.

4. Mehreen S, Khan MA, Basit A, Ashiq N, Javaid A (2015) Frequency of depression in multidrug-resistant tuberculosis patients: An experience from a tertiary care hospital. Pak J Chest Med 21: 149-54

5. Sweetland A, Acha D, Guerra D (2002) Enhancing adherence: the role of group psychotherapy in the treatment of MDR-TB in urban Peru, World Mental Health Casebook: Social and mental health interventions in low-income countries. Kluwer Academic/Plenum Press, New York 51-79.

6. Torun T, Gungor G, Ozmen I, Bolukbasi Y, Maden E, et al. (2005) Side effects associated with the treatment of multidrug-resistant tuberculosis. Int J Tuberc Lung Dis 9: 1373-1377.

7. Baghaei P, Tabarsi P, Dorriz D, Marjani M, Shamaei M, et al. (2011) Adverse effects of multidrug-resistant tuberculosis treatment with a standardized regimen: a report from Iran. Am J Ther 18: e29-e34.

8. Aamir S (2010) Co-morbid anxiety and depression among pulmonary tuberculosis patients. J Coll Physicians Surg Pak 20: 703-704.

9. Nathanson E, Gupta R, Huamani P, Leimane V, Pasechnikov AD, et al. (2004) Adverse events in the treatment of multidrug-resistant tuberculosis: results from the DOTS-Plus initiative. Int J Tuberc Lung Dis 8: 1382-1384.

10. Shin SS, Pasechnikov AD, Gelmanova IY, Peremitin GG, Strelis AK, et al. (2007) Adverse reactions among patients being treated for MDR-TB in Tomsk, Russia. Int J Tuberc Lung Dis 11: 1314-1320.

11. Furin J, Mitnick C, Shin S, Bayona J, Becerra M, et al. (2001) Occurrence of serious adverse effects in patients receiving community-based therapy for multidrug-resistant tuberculosis. Int J Tuberc Lung Dis 5: 648-655.

12. Johnson DAW (1981) Drug-induced psychiatric disorders. Drugs 22: 57-69.

13. Nariman S (1988) Adverse reactions to drugs used in the treatment of tuberculosis. Adverse Drug React Acute Poisoning Rev 4: 207-227.

14. Shin SS, Hyson AM, Castaneda C, Sanchez E, Alcantara F, et al. (2003) Peripheral neuropathy associated with treatment for multidrug-resistant tuberculosis. Int J Tuberc Lung Dis 7: 347–53.

15. Vanderpool M (2002) Resilience: A missing link in our understanding of survival. Harv Rev Psychiatry 10: 302-306.

16. Pachi A, Bratis D, Moussas G, Tselebis A (2013) Psychiatric morbidity and other factors affecting treatment adherence in pulmonary tuberculosis patients. Tuberc Res Treat.

17. Grenard JL, Munjas BA, Adams JL, Suttorp M, Maglione M, et al. (2011) Depression and medication adherence in the treatment of chronic diseases in the United States: a meta-analysis. J Gen Inter Medicine 26: 1175-1182.

18. Khan MA, Mehreen S, Basit A, Khan RA, Javaid A (2015) Predictors of poor outcomes among patients treated for multidrug-resistant tuberculosis at tertiary care hospital in Pakistan. American-Eurasian Journal of Toxicological Sciences 7: 162-172.

19. Trajkovic G, Starcevic V, Latas M, Lestarevic M, Ille T, et al. (2011) Reliability of the Hamilton Rating Scale for Depression: A meta-analysis over a period of 49 years. Psychiatry Research 189: 1-9.

20. Lau DT, Nau DP (2004) Oral anti-hyperglycaemic medication non-adherence and subsequent hospitalization among individuals with type-2 diabetes. Diabetes Care 27: 2149-53.

21. Gadit AAM, Mugford G (2007) Prevalence of depression among households in three capital cities of Pakistan; need to revise the mental health policy. PlOS One 2: e209.

22. Aghanwa HS, Erhabor GE (1998) Demographic/socioeconomic factors in mental disorders associated with TB in southwest Nigeria. J Psychosom Res 45: 353-360.

23. Aydin IO, Ulusahin A (2001) Depression, anxiety comorbidity, and disability in tuberculosis and chronic obstructive pulmonary disease patients: applicability of GHQ-12. Gen Hosp Psychiatry 23: 77–83.

24. Natani GD (1985) Depression in TB patients: Correlation with duration of disease and response to anti-tuberculous chemotherapy. Indian Journal of Tuberculosis 32: 195.

25. Sulehri MA, Dogar IA, Sohail H, Mehdi Z, Azam M, et al. (2010) Prevalence of depression among tuberculosis patients, APMC 4: 133-137.

26. Masumoto S, Yamamoto T, Ohkado A, Yoshimatsu S, Querri AG, et al. (2014) Prevalence and associated factors of depressive state among pulmonary tuberculosis patients in Manila, The Philippines. Int J Tuberc Lung Dis 18: 174-179.

27. Stewart DE, Gucciardi E, Grace SL (2004) Depression. BMC Women's Health 25: 4.

28. Duko B, Gebeyehu A, Ayano G (2015) Prevalence and correlates of depression and anxiety among patients with tuberculosis at Wolaita-Sodo University Hospital and Sodo Health Center, Wolaita-Sodo, South Ethiopia, Cross sectional study. BMC psychiatry 15: 1.

29. Orth U, Robins RW, Roberts BW (2008) Low self-esteem prospectively predicts depression in adolescence and young adulthood. J Pers Soc Psychol 95: 695-708.

30. Griffiths KM, Christensen H, Jorm AF (2008) Predictors of depression stigma. BMC psychiatry 8: 25.

31. Purohit DR (1978) Incidence of depression in hospitalized TB patients. Ind J Tuberc 25: 147.

32. Tandon AK, Jain SK, Tandon RK, Asare R, 1980) Psycho-social study of tuberculous patients. Ind J Tuberc 27: 172.

33. Morris MD, Quezada L, Bhat P, Moser K, Smith J, et al. (2013) Social, economic, and psychological impacts of MDR-TB treatment in Tijuana, Mexico: a patient's perspective. Int J Tuberc Lung Dis 17: 954-960.

34. NTP (2012) National TB control program, Pakistan.

35. Isaakidis P, Rangan S, Pradhan A, Ladomirska J, Reid T, et al. (2013) 'I cry every day': Experiences of patients co-infected with HIV and multidrug-resistant tuberculosis. Trop Med Int Health 18: 1128-1133.