"Socio-Demographic, Psychosocial Factors in MDR And XDR-Tb With Psychiatric Co Morbidities And Their Relation with Drug Adherence."

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Abstract

Aims and Objective: *To find out socio demographic profile, prevalence, adherence, type and factors associated with psychopathology in patients of MDR-TB & XDR-TB.*

Methodology: *All Indoor MDR & XDR-TB patients of a state general hospital in urban setting of western India during 1 year were enrolled. Hospital Anxiety and Depression Scale(HADS), Brief Psychiatric Rating Scale(BPRS), General Health Questionnaire(GHQ), Morisky 8-Item Medication Adherence Questionnaire(M8MAQ) were applied to assess anxiety and depression, psychosis, general health condition, treatment adherence respectively. Statistical Analysis was done to find out factors associated with psychopathology in MDR-TB & XDR-TB.*

Results: *56% (n=84) of MDR vs 62.5% (n=16) of XDR patients had abnormal scores in HADS –A subscale ; 54.8% (n=84) of MDR vs 56.3% (n=16) of XDR patients had abnormal scores in HADS-D subscale.On HADS-A subscale patients with normal, borderline abnormal and abnormal scores had GHQ mean value 10.7, 19.33, and 27.40 respectively. On HADS-D subscale patients with normal, borderline abnormal and abnormal scores had GHQ mean value 11.17, 15.22, and 27.91 respectively. Only 2.4% were noted with hallucinatory behaviour in MDR TB who were on Cycloserine.In MDR vs XDR TB patients 46.4% vs 31% and 37.5% vs 18.8% had high and medium adherence respectively. In contrast 43.8% of XDR and 22.6% of MDR had low adherence. Association of depression and anxiety with variables of sociodemographic profile were found statistically insignificant .*

Conclusion*: Illness is the only factor associated with anxiety and depression while variables like sex, occupation, marital status ,type of TB, adherence are not much important.*

Keywords*: MDR and XDR TB, Depression, Anxiety, Adherence*

I.   Introduction

Tuberculosis (TB) is a chronic infectious multi systemic disease caused by mycobacterium tuberculosis and is one of the leading causes of mortality worldwide.The literature indicates that psychiatric comorbidity before and after tuberculosis onset, psychological issues such as stigma, isolation, sense of social support, helplessness, and other psychological reactions to the disclosure of the diagnosis as well as medication side-effects, all adversely affect the treatment adherence. On the other hand, studies report high prevalence rates of psychiatric comorbidity among patients with drug-resistant tuberculosis and the prevalence of depression and anxiety significantly correlates with severity and duration of the disease. The causal relationships between mental disorders and tuberculosis are complex. Severe mental disorders are associated with high risk of tuberculosis acquisition, transmission and with poorer adherence to anti-TB treatment. Conversely, diagnosis with tuberculosis increases risk of psychiatric comorbidity.

As the prevalence of tuberculosis rises in specific groups especially among individuals who are more likely to be psychologically distressed than the general population like homeless, immigrants, and HIV patients; researchers conclude that in order to increase the cure rates of tuberculosis psychiatric, comorbidity must be identified and treated.

Although patient's perceptions about TB remain largely unknown, yet the literature shows a lot of reactions of TB patients to the disclosure of their diagnosis and these reactions included feelings of loneliness, depression, suicidal thoughts, fear, apathy, shock, concern, surprise (in relation to the lack of symptoms), and acceptation . The possible reasons for these emotions may be the stigma discrimination and social isolation attached to the disease or lack of knowledge of TB, or fear of loss of income on account of long duration of treatment." [1]

Depression and Acute stress disorder are the common stress-related conditions of TB patients. Reactions to the stressful situation brought about by the illness negatively affecting an individual's ability to work; social isolation, lowered self-esteem, fear of spreading the illness to others, helplessness brought out by

incapacitation due to severity of chronic illness, and social stigma attached to this illness, are all possible causes that one can postulate for depression and anxiety. Dependence on alcohol and other drugs could be the response to anxiety and depression [2].

Materials AndMethods

A cross-sectional study using a semi-structured questionnaire was carried out in indoor patients of TB and Chest Medicine department of a state general hospital in urban setting of western India. Patients of age between 15 to 60 years with informed consent were included in the study. Patients fulfilling criteria for Alcohol, Opium, Ganja or other substance dependence, recently diagnosed with HIV, with language barrier, not communicating in Gujarati / Hindi or English were excluded from the study.

Patients diagnosed as having MDR/XDR TB were admitted for initiation of treatment and management in TB and Chest Ward. Study enrolled all patients admitted from May 2014 to May 2015. Patients were evaluated as consecutive sampling after initial stabilization of doses. After collecting the demographic data, patients with anxiety and depression were assessed by Hospital Anxiety and Depression Scale (HADS). For assessing psychotic symptoms, Brief Psychiatric Rating Scale (BPRS) and for screening of general health condition General Health Questionnaire (GHQ-12) were used. Morisky 8-Item Medication Adherence Questionnaire, Modified Prasad Classification were used for assessing adherence to treatment and socioeconomic class respectively. After data collection patients were divided into two groups- MDR and XDR groups. Statistical Analysis was done between these two groups to find out factors associated with psychopathology in MDR-TB & XDR-TB.

Scales Administered:
Hospital Anxiety and Depression Scale (HADS)

HADS is a 14 item scale, 7 items relate to anxiety and 7 relate to depression. A number of researchers have explored HADS data to establish the cut-off points for case of anxiety or depression [3]. Through a systematic review of a large number of studies identified a cut-off point of 8/21 for anxiety or depression. For anxiety (HADS-A) this gave a specificity of 0.78 and a sensitivity of 0.9. For depression (HADS-D) this gave a specificity of 0.79 and a sensitivity of 0.83.

Brief Psychiatric Rating Scale (BPRS)

BPRS was developed primarily to assess change in psychotic symptoms in patients and covers a broad range of areas, including thought disturbance, emotional withdrawal and retardation, anxiety and depression, hostility and suspiciousness etc. Its 18 items are rated on a seven-point item-specific Likert scale from 0 to 6, with the total score ranging from 0 to 108 (in some scoring systems, the lowest level for each item is 1, and the range is 18 to 126). Reliability of the BPRS is good to excellent when raters are experienced. Validity is also good as measured by correlations with other measures of symptom severity, especially those assessing schizophrenia symptomatology. [4]

General Health Questionnaire(GHQ-12)

The 12-item General Health Questionnaire (GHQ-12) is a self-report measure of psychological morbidity, intended to detect "psychiatric disorders...in community settings and non-psychiatric settings" [5]. It is widely used in both clinical practice [6], epidemiological research [7] and psychological research [8].

Morisky 8-Item Medication Adherence Questionnaire

The eight-item Morisky Medication Adherence Scale (MMAS-8) [9] is a structured self-report measure of medication-taking behavior. This measure was designed to facilitate the recognition of barriers to and behaviors associated with adherence to chronic medications such as psychiatric drugs. The scale provides information on behaviors related to medication use that may be unintentional (e.g., forgetfulness) or intentional (e.g., not taking medications because of side effects.

II. Results And Discussion
"Table 1: Distribution of Sociodemographic profile and other variables"

Parameters	MDR	XDR
Sex Distribution		
Male	57	7
Female	27	9
Educational Status		
No Schooling	14	2

Primary School (1-8)	32	2
Secondary School	20	11
Higher Secondary School & Above	18	1
Marital Status		
Married	57	11
Unmarried	26	6
Family Type		
Nuclear	42	9
Joint	42	7
Socio-economic status		
Upper High	2	1
High	28	4
Upper Middle	27	5
Lower Middle	22	3
Poor	5	3
Occupation		
Unemployed	36	12
Unskilled labour	19	3
Skilled labour	25	1
Professional	4	0
Number of Hospital admission		
1-2 times	64	8
3-4 times	19	7
5-6 times	1	1

A total of 100 individuals(who fulfilled the inclusion criteria) were taken up for the study.84 patients had MDR TB while 16 patients had XDR TB .Nearly half of the patients of MDR i.e 42.9% (n=84) and 75% (n=16) of XDR were unemployed.During lifetime 76.19% (n=84) of MDR vs 9.52% (n=16) of XDR participants were admitted 1-2 times, 22.62% (n=84) of MDR vs 43.75% (n=16) of XDR participants were admitted 3-4times and 1.19% (n=84) of MDR vs 6.25% (n=16) of XDR participants were admitted 5-6 times due to TB in hospital [Table 1].

62% of patients were diagnosed with Tuberculosis 3 years back and started antitubercular drugs by doctors. With increasing awareness about Tuberculosis, majority of the patients started treatment with private physician but were not properly informed about the necessity of regular follow ups, total duration of treatment, prognosis and the importance of strict drug adherence. As per treating doctor majority of patients continued antitubercular drugs for a long time, but with the improvement in symptoms they discontinued treatment. With regards to overall support from family, 92% had subjective feeling of good support from family members and rated 5 in semi structured questionnaire measuring 1 to 5 in Likert scale.

"Table 2: Association between HADS-A scores and various variables"

Variables		HADS-ANXIETY (HADS-A)					
		Normal	Borderline Abnormal	Abnormal	Total	chi square	p
Sex	Male	22	5	37	64	1.325	0.51
	Female	15	1	20	36		
Occupation	Unemployed	20	1	27	48	8.075	0.23
	Unskilled	5	3	14	22		
	Skilled	11	1	14	26		
	Professional	1	1	2	4		
Education	Illiterate	2	2	12	16	10.756	0.55
	Primary	13	1	20	34		
	Secondary	13	3	15	31		

	Higher secondary	9	0	10	19		
Family	Nuclear	18	4	29	51	0.672	0.71
	Joint	19	2	28	49		
Marital status	Married	23	5	40	68	2.762	0.6
	Unmarried	14	1	17	32		
SEC	Upper high	1	1	1	3	6.523	0.589
	High	13	1	18	32		
	Upper middle	11	1	20	32		
	Lower middle	10	2	13	25		
	Poor	2	1	5	8		
Adherence	High	16	4	25	45	1.221	0.875
	Medium	11	1	17	29		
	Low	10	1	15	26		
Type of TB	MDR	32	5	47	84	0.273	0.872
	XDR	5	1	10	16		

On anxiety subscale in HADS taking the cut off score as 8/21, the range of abnormal scores was 9 to 20. 57.8% (n=64) male patients had abnormal score while 55.6% (n=36) of females had abnormal score. 56.3% (n=48) of unemployed people vs 63.6% (n=22) of unskilled worker vs 53.8% (n=26) of skilled person vs 50% (n=4) of professional had abnormal score but the results are not statistically significant. Among illiterate, primary, secondary and higher secondary and above groups 75% (n=16); 58.8% (n=34); 48.4% (n=31); 52.6% (n=19) were having abnormal scores respectively. 56.9% (n=51) of nuclear type family vs 57.1% (n=49) of joint family were found to have abnormal scores. As per modified Prasad classification for socio-economic class, 33.3%(n=3); 56.3%(n=32); 62.5%(n=32); 52%(n=25); 62.5%(n=8) had abnormal scores among upper high, high, upper middle, lower middle class and poor class respectively. 55.6% (n=45) of high adherence group vs 58.6% (n=29) of medium adherence group vs57.7%(n=26) of low adherence group had abnormal scores. [Table 2]

"Table 3: Association between HADS-D scores and various variables"

Variables		HADS-DEPRESSION(HADS-D)					
		Normal	Borderline Abnormal	Abnormal	Total	chi square	P
Sex	Male	24	4	36	64	1.655	0.437
	Female	12	5	19	36		
Occupation	Unemployed	17	5	26	48	0.987	0.986
	Unskilled	7	2	13	22		
	Skilled	10	2	14	26		
	Professional	2	0	2	4		
Education	Illiterate	3	2	11	16	9.071	0.642
	Primary	12	4	18	34		
	Secondary	12	2	17	31		
	Higher secondary	9	1	9	19		
Family	Nuclear	16	7	28	51	3.202	0.202

	Joint	22	2	27	49		
Marital status	Married	24	7	37	68		
SEC	Unmarried	12	2	18	32	2.197	0.7
	Upper high	1	0	2	3		
	High	14	1	17	32		
	Upper middle	8	5	19	32		
	Lower middle	10	2	13	25	5.209	0.735
Adherence	High	17	5	23	45		
	Medium	9	3	17	29		
	Low	10	1	15	26	1.557	0.816
Type of TB	MDR	29	9	46	84		
	XDR	7	0	9	16	2.037	0.361

On depression subscale in HADS, the range of abnormal scores was 10 to 20. 56.3% (n=64) of male patients vs 52.8% (n=36) of females had abnormal scores. 54.2% (n=48) of unemployed people ,59.1% (n=22) unskilled workers, 53.8% (n=26) of skilled persons ,50% (n=4) of professional had abnormal scores. Among illiterate, primary, secondary and higher secondary and above groups ;68.6% (n=16); 52.9% (n=34); 54.8% (n=31); 47.4% (n=19) were found to have abnormal scores respectively.54.9% (n=51) of nuclear type of family vs 55.1% (n=49) of joint family had abnormal scores .As per as marital status is concerned, 54.4% (n=68) of married persons vs 56.3% (n=32) of unmarried persons had abnormal scores. As per modified Prasad classification for socio-economic class 66.7%(n=3); 53.1%(n=32); 59.4%(n=32); 52%(n=25); 50%(n=8) had abnormal scores among upper high, high, upper middle, lower middle class and poor people respectively. 51.1% (n=45) of high adherence group vs 58.6% (n=29) of medium adherence group vs 57.7% (n=26) of low adherence group had abnormal scores [Table3]. 56% (n=84) of MDR vs 62.5% (n=16) of XDR patients had abnormal scores in HADS –A, while in HADS-D scale 54.8% (n=84) of MDR vs 56.3% (n=16) of XDR patients had abnormal scores.Whether anxiety or depression was associated with other variables like sex, occupation, education, family type, marital status, socio-economic class, adherence, type of TB or not is checked by chi square test and found to be statistically not significant (p=>0.05).

"Table 4: Association between adherence and various variables"

Variables		Adherence				chi square	P
		High (%)	Medium (%)	Low (%)	Total (%)		
SEX	Male	28(43.8)	17(26.6)	19(29.7)	64(100)	1.356	0.508
	Female	17(47.2)	12(33.3)	7(19.4)	36(100)		
Occupation	Unemployed	19(39.6)	17(35.4)	12(25)	48(100)	6.467	0.373
	Unskilled	9(40.9)	5(22.7)	8(36.4)	22(100)		
	Skilled	15(57.7)	7(26.9)	4(15.4)	26(100)		
	Professional	2(50)	0(0)	2(50)	4(100)		
Education	Illiterate	9(56.3)	3(18.6)	4(25)	16(100)	6.251	0.903
	Primary	14(41.2)	10(29.4)	10(29.4)	34(100)		
	Secondary	13(41.9)	11(35.5)	7(22.6)	31(100)		

	Higher Secondary	9(47.4)	5(26.3)	5(26.3)	19(100)		
Family	Nuclear	22(43.1)	18(35.3)	11(21.6)	51(100)	2.288	0.854
	Joint	23(46.9)	11(22.4)	15(30.6)	49(100)		
Marital Status	Married	29(42.6)	19(27.9)	20(29.4)	68(100)	3.69	0.45
	Unmarried	16(51.6)	9(29)	6(19.4)	31(100)		
	Widow	0(0)	1(100)	0(0)	1(100)		
SEC	Upper High	2(66.7)	1(33.3)	0(0)	3(100)	4.033	0.854
	High	17(53.1)	7(21.9)	8(25)	32(100)		
	Upper middle	14(43.8)	10(31.3)	8(25)	32(100)		
	Lower middle	8(32)	9(36)	8(32)	25(100)		
	Poor	4(50)	2(25)	2(25)	8(100)		
Type of TB	MDR	34(46.4)	26(31)	19(22.6)	84(100)	3.236	0.198
	XDR	6(37.5)	3(18.8)	7(43.8)	16(100)		

46.4% of MDR TB vs 37.5% of XDR TB patients were highly adherent. Whether adherence was associated with other variables of socio-demographic profile like sex, occupation, education, family type, marital status, socio-economic class, type of TB or not is checked by chi square test and found to be statistically not significant (p=>0.05)[Table 4].

"Table 5 : Distribution of GHQ and HADS-A scores"

HADS-ANXIETY	GHQ	
	mean	SD
Normal	10.7	5.115
Borderline Abnormal	19.33	1.966
Abnormal	27.40	6.954
Total	20.74	10.020

"Table 6: Distribution of GHQ and HADS-D scores"

HADS-DEPRESSION	GHQ	
	mean	SD
Normal	11.17	5.401
Borderline Abnormal	15.22	4.842
Abnormal	27.91	6.569
Total	20.74	10.020

On HADS-A subscale for assessing anxiety; patients with normal, borderline abnormal and abnormal scores were found to have GHQ mean value of 10.7, 19.33, and 27.40 respectively. On HADS-D subscale for assessing depression; normal, borderline abnormal and abnormal patients had GHQ mean value of 11.17, 15.22, and 27.91 respectively. Thus higher values in GHQ correlated with severity of anxiety or depression [Table 5 and Table 6].
Only 2 out of 84 patients of MDR had psychotic Symptoms as delusion of persecution and auditory hallucination who were on cycloserine.

"Table 7: Various studies related to psychiatric co morbidities in TB"

First author/ references	Study design	Measurement instruments	Results
Tandon et al., 1980[10]	100 tubercular patients/control group: patients undergoing treatment for long-term fever of any etiology except tuberculosis from a clinic of Tuberculosis and Chest Diseases Hospital, Allahabad.	Hamilton rating scale for depression	32% of tuberculosis patients demonstrated the presence of depression.
Natani et al., 1985[11]	150 patients of pulmonary tuberculosis admitted in Hospital for Chest Diseases and Tuberculosis, Jaipur.	Beck Depressive Inventory.	A depression rate of 49% in hospitalized TB patients, which decreased with favorable response to chemotherapy but increased in those with persistently positive sputum, up to 64%.
Meghnani et al., 1988[12]	110 hospitalised TB patients in a Chest Hospital in Jodhpur.	Hamilton rating scale for depression.	A depression rate of 53.6%.
Eram et al., 2006[13]	100 patients attending tuberculosis clinic under Rural and Urban Health Training Centre in Aligarh.	Revised Clinical Review Schedule for assessing psychiatric morbidity and the Short Explanatory Model Interview to identify patients' perspectives of	30% had anxiety or tension while 26% had loss of interest for life or depression. 6% of patient denied the diagnosis while 20% of them could not explain how they felt.

		their illness.	
Bansal et al., 2010[14]	214 outpatients registered at DOTS centre in Kanpur, India.	Cornell Medical Index and 16PF-Test FORM-A.	82.2% had psychiatric comorbidity; 85.2% had anxiety neurosis, and 14.8% had depression. On personality assessment, 54.1% were anxious, 26% introverts, 15.8% extroverts, and 4.1% had other personality traits.
Panchal et al., 2011[15]	600 patients of pulmonary TB admitted in Hospital for Chest Diseases and Tuberculosis, Jaipur.	Beck depressive inventory.	Depression was present in 82% in female tuberculous inpatients and in 52.6% in males immediately after the diagnosis.
Chandrashekar et al., 2012[16]	100 patients hospitalized for pulmonary tuberculosis in Bangalore.	MINI-International Neuro Psychiatric Interview Scale.	46% of psychiatric morbidity, majority is depressive disorders (36%) followed by anxiety disorders (24%)/comorbidity of depressive and anxiety disorders in 16% of patients.

Various studies across India showed that prevalence of depression and anxiety were common in TB patients ranging between 1/3rd to 3/4th of total study population but very few studies were done in fatal conditions like MDR and XDR TB patients exclusively [Table7]; our study focussed on prevalence, psychosocial factors affecting psychiatric co morbidities, adherence of MDR and XDR TB patients and it was found that approximately 3/5th of the study population had anxiety and depression corroborating with the previous studies but association of depression and anxiety with psychosocial factors like sex, occupation, education, family type, marital status, socio-economic class were not statistically significant.

III.   Conclusions

Socio demographic variables do not significantly affect the profiles of anxiety and depression in MDR and XDR TB patients. So illness is the only robust factor which is associated with depression and anxiety while other variables like sex, occupation, marital status ,type of TB, adherence is not much important.

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