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Research Article

Effect of Drug Abusing on Treatment Outcomes among Tuberculosis Patients with Respect to Gender Disparities

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Abstract

Background: Drug abuse has been associated with a higher prevalence of TB infection and incidence of TB disease. It is an important epidemiological factor for poor treatment outcomes among tuberculosis (TB) patients. The aim of this study was to determine the effect of drug abusing on treatment outcomes of TB patients and clinical comorbidities with respect to gender disparities.

Methods: Institution based retrospective study was conducted from January 2014 to December 2015. Data was collected for TB patients with drug abuse registered for TB treatment in a tertiary level referral hospital. Data was analyzed using SPSS version 20. Frequency, means and percentage (%) were used to present data. Logistic regression model was used to assess the association of treatment outcomes with socio-demography profile and comorbidities. P value of <0.05 was considered statistically significant.

Results: Of 850 total patients, 104 patients (12.2%) were confirmed drug abusers. Ninety-six percent of patients were male and 87.5% were diagnosed with Pulmonary Tuberculosis (PTB) cases. Around 79 patients (76%) were reported to be sputum culture or AFB smear positive. Around 37 (35.5%) were cured, 20 (19.2%) cases completed their treatment, 20 (19.2%) had interrupted treatment, while 24 patients (23%) died during treatment and 3 patients were transferred to other location. Current drug abusers 1.276 (1.108-1.453; P=<0.001), prisoners 1.572 (1.220-2.055; P=<0.001) and smokers 1.45 (1.141-1.846, P=0.002), patients with HIV sero positive status 1.269 (1.100-1.563 P=<0.001) and those with smear positive 1.517 (2.137-2.440; P=0.003) had significantly higher risk of unsuccessful treatment outcomes.

Conclusion: In the current study, the treatment success rate was lower than WHO set target. Drug abuse together with comorbidities found to have important effect on treatment outcomes among TB patients.

Introduction

Tuberculosis (TB) is potentially life threatening disease which accounts for the life quality of number of humans all over the world. One third of populations with over 1.5 million deaths annually is estimated to occur with this disease. TB is the second most frequent cause of death due to infectious agent followed by HIV/AIDs [1,2]. In spite of advance medical techniques, innovative medical approach and the implementation of World Health Organization (WHO) promoted treatment strategy like Direct Observation Therapy Short Course (DOTS) programs, TB still remains as an intense and uncontrollable disorder.

Drug abuse and Intravenous Drug Use (IDU) are recognized as significant factors in the epidemiology of TB in all over the world [3-5]. Most of the in-vitro studies have elucidated toxic effects of illicit drug abuse on human immunity [6,7]. Moreover, several studies have demonstrated a relation between complications of infectious diseases as a result of behavioral risk of drug abuse. People who use illicit drugs are frequently affected by socio-economical and clinical risk factors for TB such as to poverty, homelessness, malnutrition, hepatitis and HIV infection [8,9].

Previous literature have prominently described the role of gender disparities in drug abuser TB pandemics [10]. The concurrent abuse of alcohol and drugs continues to be a substantial problem [11]. Men are more likely to be heavy drinkers and consume larger quantities of illicit substances [12]. But somehow the trend of women participation in drug addiction is increasing day by day. One of the important reason of this increasing trend is weak neurobiological power and hormonal changes of women as having special dilemma which stem from basic issues like estrogen level, depression, sexuality, low self-esteem, relationships, physical or sexual abuse, emotional exposure, childhood experiences [13].

Comorbidities such as HIV infection, chronic kidney disease (CKD) and diabetes mellitus (DM) are reported to have poorer treatment outcomes among TB patients somewhere else [14]. In general, there is lack of research on comorbidities and treatment outcomes among TB patients in Malaysia. Therefore, the main objective of this study was to determine the effect of socio-demography and co-morbid conditions on treatment outcome among TB patients with drug abuse.

Materials and Methods

Study design: This study was retrospective observational study conducted among the TB cases registered at the General Hospital Penang. The study population included illicit drug abusers who underwent TB treatment based on both definite and provisional diagnosis from January 2014 to December 2015. The medical record of TB patients was contained in an envelope which was referred to as the patient case. Socio-demographic profile and clinical characteristics recorded and compared among male and female patients. Standard TB treatment that comprises Isoniazid (H), Rifampicin (R), Ethambutol (E) and Pyrazinamide (Z) (HREZ) were given for two months intensive phase followed by continuous phase of at least four months with regimen of HR to all TB patients. Substance abuse was defined as

self-reported acute alcohol use, drug use by injection, or non-injection drug use during the year before TB diagnosis. Treatment outcomes were defined based on WHO criteria [15].

Successful treatment outcomes: Cured and treatment completed were recorded as successful treatment outcomes. Unsuccessful treatment outcomes: included died, defaulted and treatment failure.

Statistical analysis: The whole data collection forms were assigned a serial number to ensure the traceability. Coding of the responses were carried out and the data entered into computer and analysed by using statistical package for social science (SPSS) software programme for windows version 20.0 (SPSS, Inc, Chicago, IL, USA). Frequency, mean, percentage (%) and standard deviation (SD) were used to express data. Patients demographic data was entered as categorical variables. Categorical data was presented as percentage and frequencies, while continuous data was reported as mean and standard deviation (SD). Chi-square and fisher exact tests were used to note significance between categorical variables. Logistic regression was used to indicate significance of association between independent and dependent variables. P value <0.05 was considered statistically significant.

Results

Socio-demographic and clinical findings of drug abuser TB patients. Total 850 TB cases were registered during the study time period. One hundred four of these total patients (12.2%) were confirmed drug abusers including 100 (96.2%) males and 4(3.8%) females. The male gender ratio among TB and IVDU was high as compared to females. Around 79% patients were aged>35 years. Table 1 presents the socio-demographic characteristics of study subjects. The mean body weight was recorded as 51.5 ± 11.6 Kg.

The ratio of drug abusing patients differed considerably across demographic and clinical characteristics. As consider race, the majority of patients reported as drug users were Malays and Chinese, followed by Indians. Significantly higher percentage of these patients was unmarried (71%). About 55.8% drug abusers were unemployed, 89.4% had smoking habit, and 57.6 % had previous record of abusing illicit drugs. Mostly observed drug used was heroine chasers 53 (51%). Followed by patients who were abuser of both IVDU and heroine.

Disease status and co-morbidities

The clinical characteristics of drug abusers with co-morbid conditions are shown in Table 2. Majority of drug addicts were diagnosed with PTB (96.7%) whereas EPTB was diagnosed in 13 cases (12.5%). Seventy-nine cases (76%) were found to be sputum culture or acid fast bacilli (AFB) smear positive with highest percentage among male patients. Compared to TB-HIV, the occurrence of TB-Hepatitis was higher among drug abusers (53.8%). Males were more likely to have increased risk of co-morbidities as compared to females.

Association of socio-demographics with treatment outcomes

Table 3 shows regression analysis of treatment outcomes with different socio-demographic characteristics. On multivariate analysis, currently drug abusers 1.276 (1.108-1.453), prisoners 1.572 (1.220-2.055) and smokers 1.45 (1.141-1.846) had significantly positive association with unsuccessful treatment outcomes.

Association of comorbidities with treatment outcomes

A correlation was drawn between treatment success rate against disease status and co-morbidities. Patients who had positive significant association with unsuccessful treatment outcomes were those with sputum smear positive 1.517 (2.137-2.440) and HIV co-infection 1.269 (1.100-1.563) (Table 4).

The rate of successful treatment outcomes was more than was recorded as 54.7%. Male TB patients were more likely to be cured as compare to female. Around 37(35.5%) were cured, 20(19.2%) cases completed their treatment, 20(19.2%) had interrupted treatment, while 24 patients (23%) died during treatment and 3 patients were transferred to other location.

Discussion

Malaysia is a country comprising of three main races including Malays, Chinese and Indians. In a study conducted in Malaysia, 16.8% TB patients were found to be drug abusers with mostly being Malays [16]. Majority (78.8%) of TB drug users were above 35 years of age group in the present study.

There are different findings with respect to drug abuse among different age group. Some of the studies have reported increased use of illicit substances among young adults [17] while others have observed among old age people [18].

In this retrospective observational study we studies gender disparities with regard to socio-economic and clinical characteristics and their effect on treatment outcomes. This study revealed high ratio of TB among males than females. These findings are consistent with WHO statistics and other studies [19-22]. Numbers of studies have indicated that socio-economic risk factors contribute differently in developing TB among males and females. Most commonly reported risk factors include smoking, alcoholism, male sex, overcrowding, silicosis, diabetes and poverty [19,23]. M. *tuberculosis* exposure differs on gender basis owing to differences in risk behaviors, social roles and activities. Males often travel more; may have more social contacts; spend more time in settings that may be favorable to transmission, such as bars; and are frequently engaged in occupations associated with a higher risk for TB, such as mining [24]. Drug abuse has also been termed as an important factor in the epidemiology of TB in developed and developing countries [25]. The environmental and physiological effects of drug abuse in addition to high risk behaviors may contribute to high prevalence of TB among drug users. deleterious effects of drug use on human immune system are well reported [6]. In our study 104/850 (12.2%) TB patients were reported as current drug abusers. A study conducted in Brazil among TB patients discovered 15.3% TB patients as drug abusers of total studied population [26]. Beside this, another oeltmann et al. (2009) reported drug abuse as greater risk factor TB with a percentage of (18.7%) among patients [27].

In the present study, proportion of PTB patient was high among study cohort as compared to EPTB patients. However, lower success rate of TB treatment (38.4%) was noted among EPTB patients and 52% for PTB patients; however, the difference was not significant. These findings are supported by studies conducted elsewhere [20,21,28]. The reason for this might be delayed diagnosis of EPTB as compared to PTB because definitive and rapid diagnosis of EPTB is challenging as tissue samples are difficult to procure for diagnosis and clinical presentation is atypical. Another difficulty is that EPTB specimens

usually yield very few bacilli and associated with low AFB smear and culture [29].

The use of illicit drugs has been associated with slightly higher trends of non-adherence to anti-TB treatment [30]. In present study, prisoners, drug abusers, smokers, patients with sputum smear positive, and HIV co-infection, significantly had increased risks of unsuccessful treatment outcomes. A previous study conducted in Ethiopia also discovered higher defaulting rate of anti-TB treatment among smear positive TB patients [31]. The default rate among TB smear positive drug abusers found in current study was similar to that found in another study conducted in Malawi. This can be due to cavitation associated with higher baseline sputum bacterial load. Patients with heavy bacillary load at baseline are more likely to have delay in sputum conversion at the end of the intensive phase of TB treatment, and delay in sputum conversion is independently associated with treatment failure and death [32]. The odds of having unsuccessful TB treatment outcome were 1.2 times higher among TB-HIV co-infected than HIV negative TB patients similar to the findings from Eastern Ethiopia, Benin and Malawi [33-35]. This might be due to low level of immunity and drug mal absorption [36], resulting in ADRs and ultimately drug resistance [37].

In parallel to the present findings, prisoners are identified as independent risk factor for unsuccessful treatment outcomes of TB [38]. Prisons are increasingly becoming ideal breeding grounds for the concentration and dissemination of TB (including multidrug-resistant TB [MDR-TB], from which infection is transmitted to the general population. Active transmission of drug-resistant strains, overcrowding and poor living conditions, limited health care, including inadequate TB treatment and control strategies, and the spread of HIV infection, are factors contributing to the disproportional burden of TB in prisons [39]. Findings from the current study proved smoking to be one of the main factors associated with unsuccessful treatment outcomes of TB therapy [40,41].

Conclusion

In the current study, the treatment success rate was 54.7%, lower than WHO set target. The present study suggests drug abuse together with its related socio-demographic and clinical characteristics as risk factors for unsuccessful treatment outcomes among TB patients. TB control and drug abuse programs may work together to deal such issues globally.

Ethical approval

Ethical clearance was secured from all relevant authorities and Clinical research centre (NMMR-16-2617-33729(IIR).

Variables	Total 104 (%)	Male 100 (96.2%)	Female 4 (3.8%)
Age (years)	46.4 ± 12.8	46.6 ± 12.8	40.7 ± 14.1
Mean age	22 (21.2)	21 (95.4)	1 (4.5)
Below 35	82 (78.8)	79 (96.3)	3 (3.6)
Above 35			
Body Weight (Kg)	51.5 ± 11.6	51.6 ± 11.6	48 ± 12.2
Mean Weight			
Race	36 (34.6)	35 (97.2)	1 (2.7)

Malays	29 (27.8)	28 (96.5)	1 (3.4)
Indians	36 (34.6)	35 (97.2)	1 (2.7)
Chinese	3 (2.8)	2 (66.6)	1 (33.3)
Others			
Marital Status	30 (28.8)	28 (93.3)	2 (6.6)
Married	74 (71)	72 (97.2)	2 (2.7)
Unmarried			
Employment Status	46 (44.2)	45 (97.8)	1 (2.1)
Employed	58 (55.7)	55 (94.8)	3 (5.1)
Un Employed			
Drug Abuse Status	44 (42.3)	42 (95.4)	2 (4.5)
Current	60 (57.6)	58 (96.6)	2 (3.3)
Ex			
Prison Status	32 (30.7)	32 (100)	0
Yes	72 (69.2)	68 (94.4)	4 (5.5)
No			
Smokers	93 (89.4)	89 (95.6)	4 (4.3)
Yes	11 (10.5)	11 (100)	0
No			
Illicit Substances	53 (51)	49 (92.5)	4 (7.5)
Heroin	26 (25)	26 (25)	0
IVDU*+heroin	14 (13.5)	14 (13.5)	0
Cannabis	11 (10.6)	11 (10.6)	0
Methamphetamine			

Table 1: Socio-demographic status of patients, Intravenous drug users*.

Variables	Total 104 (%)	Male 100 (96.2%)	Female 4 (3.8%)
Diagnosis	88 (84.6)	86 (97.7)	2 (2.2)
Definite	16 (15.3)	14 (87.5)	2 (12.5)
Suspected			
TB* Type	91 (87.5)	88 (96.7)	3 (3.2)
Pulmonary	13 (12.5)	12 (92.3)	1 (7.6)
Extra Pulmonary			
TB Smear Test	79 (75.6)	78 (98.7)	1 (1.2)
Positive	25 (24)	22 (88)	3 (12)
Negative			
Hepatitis	59 (53.8)	58 (98.3)	1 (1.6)
Positive	45 (43.2)	42 (93.3)	3 (6.6)
Negative			
HIV** Status	15 (14.2)	14 (93.3)	1 (6.6)
Positive	89 (85.5)	86 (96.6)	3 (3.3)
Negative			

Table 2: Disease status and co-morbidities among patients with drug abuse. Tuberculosis* Human immunodeficiency virus.**

Variables	Univariate analysis COR* (95% CI**)	P-value	Multivariate Analysis AOR***(95% CI)	P-value
Gender Male Female	1.137(0.862 to 2.005) 1	0.860	-----------------------	--------
Age (years) Below 35 Above 35	2.041(0.745 to 5.526) 1	0.068	-----------------------	--------
Race Malay Indians Chinese Others	1.244(0.550 to 2.814) 1.850(0.760 to 4.503) 0.527(0.233 to 1.193) 0.402(0.035 to 4.574)	0.599 0.175 0.124 0.462	-----------------------	--------
Marital Status Married Un Married	1.387(0.362 to 5.305) 1	0.433	-----------------------	--------
Employment Status Employed Un Employed	1.556(0.710 to 3.409) 1	0.008	-----------------------	--------
Drug Abuse Current Ex	1.173 (1.032 to 1.338) 1	0.003	1.276 (1.108-1.453)	< 0.001
Prison Yes No	1.912 (1.537 to 2.480) 1	0.015	1.572 (1.220-2.055)	< 0.001
Smokers Yes No	1.522 (1.234 to 1.841) 1	< 0.001	1.45 (1.141-1.846)	0.002

Table 3: Logistic regression analysis for association of socio-demographic characteristics with unsuccessful treatment outcomes. Crude Odd Ratio* Confidence Interval** Adjusted Odd Ratio.***

Variables	Univariate analysis COR***(95% CI)	P-value	Multivariate Analysis AOR****(95% CI)	P-value
Diagnosis Definite Suspected	1.692 (0.578 to 4.952) 1	0.337	------------------	--------
TB* type Pulmonary Extra Pulmonary	0.729 (0.222 to 2.399) 1	0.603	------------------	--------
TB Smear Test Positive Negative	1.674 (0.816 to 2.396) 1	0.009	1.517 (2.137-2.440)	0.003
Hepatitis status Positive	2.102 (0.954 to 4.623) 1	0.017	------------------	--------

Negative				
HIV[**] Status Positive Negative	1.178 (1.034 to 1.448) 1	0.003	1.269 (1.100-1.563)	<0.001

Table 4: Logistic regression analysis for association of disease status and co-morbidities with treatment outcomes. Tuberculosis[*] Human immunodeficiency virus[**]Crude Odd Ratio[***]Adjusted Odd Ratio.[****]

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