

Full Length Research Paper

Factors associated with default from treatment among tuberculosis patients in Kassala State, Sudan 2013

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Sudan, particularly the eastern part shoulders 8% of TB burden in the World Health Organization (WHO) Eastern Mediterranean Region (EMR). Kassala state is classified as one of the most tuberculosis (TB) affected states in Sudan with annual risk of around 120 new cases per 100,000 of populations. TB medications take a relatively long time to ensure adequate treatment. Default from TB treatment leads to continuation of disease transmission and multidrug resistant TB cases. Default rate in Kassala state is 11% while the globally acceptable rate is below 4%. This study aimed to find out the main risk factors associated with default from TB treatment among pulmonary TB patients in Kassala state in 2013. The study used case control design with (102 cases and 204 controls), structured questionnaire was used to collect socio-demographic factors. Multivariate logistic regression analysis model was built to quantify the association between risk factors and study outcome. Male to female ratio was 3:2, with age ranges between 15 and 85 years and the mean was 44 years \pm 17.4 years. Stopping treatment after feeling improved and completing the intensive treatment phase was an important predictor of defaulting. Age and education level are found to be negatively associated with the default from the TB treatment. Stigma was also found to be strongly associated with the default rate. The current DOTS strategy and its components should be further strengthened by raising attention of medical personnel towards the strategy. An effective communication channel between the care provider and the patient should be maintained to better education and ensuring of maximum adherence to treatment regimen.

Key words: TB default, DOTS strategy, stigma, case control.

INTRODUCTION

Tuberculosis (TB) is second killer worldwide due to a single infectious agent (Lozano et al., 2013). In 2011,

8.7 million people fell ill with TB; 1.4 million had already died from it and over 95% of TB deaths occur in low and

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middle-income countries. In 2010, there were about 10 million orphan children as a result of TB deaths among parents. In Sub-Saharan Africa an estimated 17 million people were infected with *M. tuberculosis* the incidence of TB has been rising upward, as reflected in estimates derived from population-based surveys and from routine TB surveillance data (Dye and Borgdorff, 2010). Sudan shoulders 8% of TB burden in the WHO Eastern Mediterranean Region (EMR) (Mohamedsalih, 2011). Tuberculosis is a major cause of morbidity and mortality in Eastern part of the Sudan. According to National Tuberculosis Program (NTP), Kassala is classified as one of the most suffering states in Sudan from the burden of tuberculosis infection. In Kassala State, annual risk of TB infection is estimated by 120 new cases per 100,000 populations (National TB Program, 2012). The TB epidemic is an outgrowth of the longstanding wars in the region (Ethiopian/Eretria, Eastern front conflict), which has gravitated poverty, malnutrition, and increased number of displaced populations and refugees in the state. This resulting in poor health infrastructure with lack of microscopic services and health personnel that also contributed to the epidemic (Rodier et al., 1993). Several countries have surpassed the global target for treatment success of 85% in 2005. In 2010 the target for success has been raised to 90% (Sudan TB Program, 2011). In Sudan the treatment success rate remained static at a rate of 80% to 82%. The main barrier for achieving the desired success rate is the high default rate. It increased from 10% in the 2008 to 11.9 in 2010; and when it combined to transfer-out it equals 16.1% (1246 out of 7729 patients registered) (Zumla et al., 2013). Default rate in Kassala State is estimated by 11 and 16% if adding the transfers (Sudan TB Program, 2012). These figures are relatively high in comparison to other countries in the region (which have default rates of 1 to 13% that include transfers). WHO and the Sudan TB treatment protocol have defined defaulting as a "treatment interruption of two consecutive months or more" (Brasil and Braga, 2008). WHO defines transfer out "as a patient who has been transferred to another recording and reporting unit and whose treatment outcome is unknown". The national target of TB control program in Sudan is to achieve 4% default rate from the current rate of 11.9%.

Causes of non-adherence to anti-TB drugs have been studied worldwide; a review of several studies (mostly from low and middle income countries) reflected the complex nature of the adherence to treatment and how it is influenced by the interaction between different factors. The factors that influence adherence were categorized into structural factors (including poverty, especially costs, financial burden and gender discrimination) (Chani, 2010), personal factors (including knowledge, beliefs and attitudes towards treatment, interpretation of illness and wellness), social context (incorporating support from the family and the community and stigma), health services factors (incorporating organization of care and treatment, disease progress and side effects). Few studies were

conducted in Sudan to investigate reasons of high default rate. One study was carried out in Khartoum state and other one was carried out in Sinnar State (Eltilib et al., 2010). Another study conducted to figure out the reasons associated high Tuberculosis default rate in Sinnar state which was reaching up to 20% of total reported treatment outcome. The study had shown that patient awareness concerning TB duration was topped the reasons of high default rate, and it followed by socio-economic factors and geographical factors. This study aimed to identify the most important factors influencing TB treatment default in Kassala state in the eastern part of the country.

MATERIALS AND METHODS

Study design and population

It was case control study design (102 cases and 204 controls). Total coverage sampling technique was applied to include all defaulters registered in Kassala State during 2012 to 2013. The inclusion criterion and definition of cases was a Pulmonary TB patient who defaulted from the treatment for 2 consecutive months as per WHO definition. The study has excluded all severely ill patients and the ones who have extra-pulmonary manifestations of TB. Controls defined as pulmonary TB patients who successfully completed their treatment in the same period in Kassala TB centers. Controls were TB patients and had been randomly recruited in the study from the sampling frame (clinical registers) without matching with the cases.

Study area

Kassala State is one of the eastern Sudan states encompassing 11 localities. Kassala is bordered by Eritrea and Ethiopia to the east, Red sea state to the north, Khartoum and River Nile states to the west and Gadarif state to south west. Land space is 42,282 km (Sq) and total population of 1,881,510 with average family size of 6.3.

Sample size

Using total coverage technique, total 102 defaulters were included with 204 controls; in 1:2 ratio to increase the statistical power of the study) (Rothman et al., 2008).

Data collection and processing

Data was collected through a structured questionnaire for required socio-demographic factors and reviewing patient registry to check eligibility through their continuation and history of treatment. Since TB is a stigmatizing disease reporting bias was expected to affect participant's responses. In order to overcome the expected reporting bias the selected data collectors were basically counsellors working within these TB centers. Patients felt that their confidentiality was preserved and their acceptance to participate in the study was probably made easier. The data from these two sources was processed; double entered and checked using the SPSS version 19 software. Multivariate logistic regression model was built to quantify the strength of association between risk factor and study outcome. Adjusted OR was calculated taking patients who have successfully completed the treatment course as a reference (Peng et al., 2002). Ethical approval was obtained from

the ethical review committee in Sudan National Board of Medical Specialization and Sudan Federal Ministry of Health (FMOH); informed consent was obtained from all study participants.

RESULTS

Baseline characteristics of the study participants

301 subjects were included in the analysis of this study, 102 (34%) were cases and 199 (66%) were controls. Overall response rate was 98%. 182 (60.5%) of participants were males and 119 (39.5%) were females. Age ranged from 15 to 85 years with mean 44.03 and $STD \pm 17.44$. More than half of them (51.7%) had their age between 31 to 60 years. They belonged to different tribes of the eastern Sudan, most of them; 178 (59.3%) were Beja, 196 (65.1%) were from urban areas while 105 (34.9%) were from rural areas. Majority of the study participants 213 (70.8%) are married. Majority of participants have education status below secondary school and most of them were daily wage workers or have no current job. The distribution of baseline characteristics of cases and controls are summarized in Table 1.

Factors associated with defaulting from TB treatment

A multivariate logistic regression analysis model was built using the enter method for the statistically significant variable at the univariate analysis level taking P value of 0.25 as a cutoff point for inclusion in the main effect logistic regression model as proposed by senior statisticians (Hosmer et al., 2013). The logistic regression model used to calculate adjusted odds ratio by taking patients who have successfully completed their treatment course as a control group. In the final model there are four variables that found to be statistically significant with P value less than 0.05. The most important and most strongly associated factor with the outcome is stopping the treatment after feeling improved and completing the intensive treatment phase (OR = 7.28, 95% CI: 4.2 to 12.6 and P value < 0.001). Age is found to be negatively associated with the default from the treatment after adjusting for the other study variables, (OR = 0.98; 95% CI: 0.96 to 0.99 and P value 0.02). Also education level of the TB patient is found to be strongly and negatively associated with the default rate (OR = 0.37; 95% CI: 0.16 to 0.89 and P value 0.02). One stigma variable was found to be significantly associated with the default rate when controlling for all other variables, patient feeling shame from TB is strongly predicting the default (OR = 2.3; 95% CI: 1.2 to 4.3 and P value 0.01). Patient hide TB infection status, patient social isolation after being diagnosed as TB case were and patient knowledge regarding treatment duration were not statistically significant. Table 2 summarizes the multivariate logistic regression model for risk factors and TB treatment default.

DISCUSSION

Stopping TB treatment after patient feeling improved and completing the intensive treatment phase was found to be the strongest statistical predictor for defaulting; the probability of stopping treatment after feeling improved was seven times higher. This finding was observed as well in several studies such as those which were carried out in Ghana, Nigeria and Kenya during 2005 to 2011 (Gupta et al., 2011; Dodor and Afenyadu, 2005; Daniel et al., 2006; Muture et al., 2011). Taking into account the long duration of anti-tuberculosis treatment and rapid response after initial phase, the authors were quite concerned about the knowledge of the study participant regarding TB treatment duration. Since this finding might be related to lack of awareness or inadequate knowledge regarding the treatment, the authors decided to keep the variable of patient knowledge about the treatment duration at all steps and levels of logistic regression model building, taking it as a biologically important variable although it was not showing any statistical significance.

Age of participants is found to be negatively associated with the default from the treatment after adjusting for the other study variables. In the final logistic regression model, age was dichotomized taking 40 years (around the average) as a cutoff. Older patients were found to have less default rate, although it is a weak association since the OR is approaching the null value. This finding is consistent and coherent with several studies cited from deferent parts of the world and at the same time is contradicting other studies findings. This point was discussed also in Ghana study which was conducted in 1990 (Van Der Werf et al., 1990).

Education level of the TB patients was found to be strongly and negatively associated with the default rate. In this study education level was dichotomized in two categories taking secondary education as a cutoff. So, patients with education level of at least secondary are found to be having around 60% less chance to default compared with those having education level less than secondary level. This finding is also supporting the study hypothesis and coherent with several literature such as the study which conducted in six Russian regions in 2007 (Jakubowiak et al., 2007). Stigma is found to be strongly associated with the default rate when controlling for all other variables, patient feeling shame of TB is strongly predicting the default compared to others who don't feel shame of having TB. This finding was largely concluded by several authors studding the same hypothesis such in South Africa and Egypt in 2002 and 2013 respectively (Finlay et al., 2012; El-Din et al., 2013). Other socio-demographic factors were found not to have influence on treatment default. These factors include patient hide TB infection status, patient social isolation after being diagnosed as TB case, marital status, residence, income, distance from TB center, cost of travel to the health center, family and social support and waiting time in TB

Table 1. Distributions of the study population by baseline characteristics, Kassala State, 2013.

Parameter	Defaulters		Controls	
	No.	%	No.	%
Male	58	56.9	124	62.3
female	44	43.1	75	37.7
Residence:				
Rural	42	41.2	63	31.7
Urban	60	58.8	136	68.3
Age:				
≤ 20 yrs	12	11.9	16	8.1
21 - 30	23	22.8	38	19.3
31 - 40	20	19.8	30	15.2
41 - 50	21	20.8	38	19.3
51 - 60	15	14.9	30	15.2
≥ 61 yrs	10	9.9	45	22.8
Tribe:				
Hadandwa	40	39.2	38	19.2
Beni Amir	32	31.4	68	34.4
Hawsa	15	14.7	24	12.1
Halanga	04	3.9	20	10.1
Rashayda	02	2.0	10	5.1
Others	09	8.8	38	19.2
Education:				
Below secondary school	90	88.2	149	74.9
Secondary and above	12	11.8	50	25.1
Occupation:				
Employee	1	1.0	6	3.0
Daily worker	50	49	96	48.2
Not work	47	46.1	86	43.2
students	4	3.9	11	5.5
Marital status:				
Single	28	27.5	45	22.6
Married	68	66.7	145	72.9
Divorced and widowed	06	5.9	09	4.5
Income:				
Less than 400 SDG	41	48.8	70	42.7
400 - 670 SDG	26	31	56	34.1
More than 700	17	20.2	38	23.2

center. Since it was a case control study, the inherited limitation of recall bias is possible; however in this study it is expected to be of limited effect since the study duration was not so long and both cases and controls were having patient's follow-up cards and registers. Selection bias could have a role in estimated measurement of association in this study, it was attempted to address it by

total coverage of all defaulters and random selection of controls with 1:2 ratio.

CONCLUSION

Stopping treatment after feeling improved, age, education

Table 2. Distribution of Logistic Regression Multivariate analysis for risk factors associated with default from TB treatment, Kassala State, 2013.

Variable	P-value	OR	95% CI	
			Lower	Upper
Age of participants in years:				
< 40	0.02	0.98	0.963	0.997
≥ 40				
Education level:				
< secondary	0.02	0.373	0.162	0.859
≥ secondary				
Stopped treatment after feeling improved:				
Yes	0.00	7.278	4.177	12.6
No				
Feeling shame of having TB:				
Yes	0.01	2.252	1.182	4.28
No				
Patient hides his infection from others:				
Yes	0.35	1.476	0.766	2.84
No				
Patient knowledge about treatment duration:				
Yes	0.90	1.077	0.357	3.25
No				

Statistical cutoff P-value for inclusion in multivariable model is 0.25, P-value of ≤ 0.05 is considered statistically significant for association between risk factor and outcome.

level and stigma are the factors associated with the default from the TB treatment in eastern part of Sudan. TB control program should maintain an effective communication channel between health facilities and patients during the treatment phases. More focus on the period after the initial intensive phase and patient feeling improved. Younger age TB patients should have special focused activities to keep their adherence to treatment. An ultimately the current DOTS strategy and its components are the target to be strengthened in the eastern states of Sudan with more health educational aspects.

Conflicts of interest

Authors disclosed that there are no financial or other relevant competing interests.

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