Social Determinants: Reinforcing and Enabling Factors as Predictors of Treatment-Adherence in Community-Based Drug Resistant Tuberculosis Patients in South-West, Nigeria

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Abstract

Background: Medication Non-adherence in the treatment of patients with Tuberculosis (TB) is a major challenge in community-based clinical therapeutics. This has been attributed, in part, to duration and complexity of treatment regimens and toxic side-effects, which facilitates disease transmission with emerging resistance to anti-TB drugs. This study was undertaken to assess level of adherence to treatment and identify social determinants moderating medication-adherence guided by the PRECEDE framework among patients receiving treatment in South-west zone of Nigeria.

Method: This was a cross-sectional survey design conducted as a community-based study with 226 consenting patients receiving second-line drug treatment based on data obtained from all DR-TB OPD Health facilities within South-west, Nigeria. The study adopted total enumeration sampling technique. Data analysis was performed using IBM SPSS version 22. Univariate and multivariate Regression analysis was conducted to validate the association between the independent variables (Reinforcing and Enabling factors) and outcome variables (medication- adherence and appointment keeping behavior). The test of significance was set at 5% for all statistical procedures.

Results: Male participants in this study was 61.3%. Mean treatment-adherence prevalence was 84.75% (20.34 \pm 3.37 measured on 24-point scale). Social/Environmental factors correlated positively with treatment -adherence (r=0.165; p<0.01). Enabling factors with OR=1.44 (95% CI=1.08-1.92, p=0.013) predicted treatment-adherence more significantly than reinforcing factors for participants in this study.

Conclusion: Patients' level of treatment-adherence was fair. Special attention should be given to enabling and reinforcing factors during patient education through social learning and structural support, which the study identified as inadequate, to optimize treatment-adherence in DR-TB patients.

Keywords: Reinforcing, Enabling, Drug resistance, Tuberculosis, Treatment-adherenc.

Introduction

Tuberculosis is a chronic infectious disease which is often strongly associated with overcrowding and poverty. Poverty directly accounts for almost one third of the global burden of disease. Poverty leads to poor health and this in turn aggravates poverty and reduce human productivity. While under-researched, poverty and low socio-economic status are associated with worsening treatment outcomes for those with TB (Lönnroth et al., 2010). Risk of exposure to Mycobacterium tuberculosis (MTB) is dependent on social and risk behaviours such as living or working in high incident settings, overcrowding with poor ventilation that increases the risk of exposure (Baker *et al.*, 2008). Poverty and low socio-economic status are factors linked to the causal pathway that directly increase the risk of being infected (exposure to infectious sources) or developing TB (impairment of the immune defence system). Malnutrition increases the susceptibility to disease; income constraints can limit the use of health care services (Duarte *et al.*, 2018).

Over the years, there has been increasing evidence of the role of socioeconomic factors on health and TB epidemiology. Therefore, focus should no longer be only on health outcomes, but at the root causes of poor health by understanding the social and physical conditions in which people live as measures of community health. These conditions affect health and well-being broadly. It predisposes some communities to better health and placing obstacles to health for others through unequal distribution of these conditions (Healthy people, 2020).

Although Directly observed treatment shortcourse (DOTS) has pioneered the use of a patient's social network to improve treatment adherence, a social determinant's framework also highlights how being driven by poverty, lack of hope for the future, might also foster high rates of treatment default that undermine TB control (Hargreaves *et al.*,2011).

Adherence to most drug regimens is poor across all populations and all diseases especially chronic illnesses such as diabetes, TB, and cardiovascular diseases. Among patients with chronic illnesses, approximately 50% fail to take medication as prescribed (Brown & Bussell, 2011). Consequently, poor adherence to TB medication leads to poor clinical outcome, increase in morbidity and mortality with an estimated 2-5% loss to GDP at a cost of \$100 trillion incurred by 2050 (Bosworth *et al.*, 2011; WHO Global TB strategy, 2019).

Greater than 80% adherence based on number of pills taken is considered successful for most chronic diseases (Osterberg & Blaschke, 2005). A myriad of factors are responsible for poor medication adherence and include those that are related to patients (e.g. suboptimal health literacy and lack of involvement in the treatment decisionmaking process), those that are related to physicians (e.g. prescription of complex drug regimens, communication barriers, ineffective communication of information about adverse effects, and provision of care by multiple physicians), and those that are related to health care systems (e.g. office visit time limitations, limited access to care, and lack of health information technology).

One of the major obstacles in treating TB patients is their non-adherence to the treatment regimen and this results in prolonged disease transmission and development of resistance to the anti-TB drugs. Treatment adherence is a critical determinant of successful TB control. Adherence to long course drug resistant TB treatment is a complex, dynamic process with wide range of factors impacting on treatment taking behaviour (Munro *et al.*, 2007). Therefore, a combination of methods which impacts on treatment taking behaviour may be required to improve patient

adherence. Although there is no gold standard for assessing adherence, properly implemented validated tools and assessment strategies can prove valuable in most clinical settings.

Various methods have been used to measure adherence and can be broadly categorized into direct and indirect measures. Direct measures involve measuring the concentration of drug levels in the blood or urine which provides proof of intake of the last few doses and directly observed therapy. It is unclear that DOT results in better treatment outcomes when compared to selfadministered therapy. The DOTS is а multipronged intervention strategy of which direct observation of therapy is just one component. It also encompasses the use of shortcourse therapy, use of smear microscopy for diagnosis and systematic reporting of treatment outcomes (Obermeyer et al., 2008). In a recent systematic review, the value of DOTS has been questioned in which it was suggested that direct observation of treatment is unnecessary and disrespectful of patient as this may result into loss of time, autonomy and privacy; regular travel to a health facility may also lead to loss of money and employment (Tian et al., 2014; Yellappa et al., 2016; Subbaraman et al., 2018). Both selfadministered treatment and treatment observation by a family member or relatives have been proposed as acceptable alternatives.

The aim of this study was to assess the level of adherence to treatment modality and identify social determinants of health associated with drug resistant TB treatment adherence in the homebased DOT strategy guided by the health behaviour theory and model of the PRECEDE meta-model in the south-west zone of Nigeria. This meta-model is an existing conceptual framework by Green & Kreuter, the Predisposing, Reinforcing. Enabling Constructs in Educational/Environmental Diagnosis and Evaluation (PRECEDE) model has successfully provided understanding of problem dynamics in resolving health challenges and preventing or controlling diseases by defining an ecological perspective to conduct scoping of the problem phenomenon. A better understanding of the social determinants of treatment adherence in drug resistant TB patients is necessary to design effective interventions that might help reduce morbidity and mortality and thereby improve treatment success. It is hoped that insights gained from this study would help optimise gains in TB

enrolment, treatment and cure rates which are not uniform between male and female.

Methods

Study design

This was a descriptive cross-sectional survey study based on data obtained from questionnaires administered to DRTB patients in South-west, Nigeria. The study design was chosen to provide data on the entire population under study and to help identify factors that may be associated with treatment adherence in community-based DR-TB patients at a specific point in time.

Study area

The study was carried out in all primary, secondary and tertiary health facilities attending to community/home- based DR-TB DOT patients during their monthly out- patient clinic visits. All health care facilities meeting these criteria were located in South-west geographical zone of Nigeria.

Study population

The targeted study population were patients receiving second line DR-TB drug treatment from designated DR-TB outpatient department (OPD) health facilities within South-west Nigeria. These are patients receiving free drugs and treatments.

Inclusion Criteria The population of interest in this study were new or re-treatment TB patients diagnosed with drug resistant TB who implement home-based DOTS treatment strategy and attend monthly follow-up OPD clinics in the hospitals selected. Only patients who had been on full course of DR-TB treatment for at least one month prior to the study and were physically, mentally capable of providing informed consent were recruited for the study. Patients aged 18 years or older who were currently receiving drug resistant TB treatment and had accepted to participate in the study were considered eligible for the study.

Sample size and sampling methods (Techniques)

The study adopted total enumeration sampling technique of home or community based DRTB patients attending monthly OPD clinics in all OPD facilities found in South-west, Nigeria. Total population sampling is a type of purposive sampling where the whole population of interest is set apart by an unusual and well-defined characteristic. Sampling was not done since all patients fulfilling the eligibility criteria were approached for the study. The target group was small and with only a few participants meeting the eligibility criteria. Therefore, sample size computation was not required based on patient records kept by the state TB programs in the respective states. Patient that met the eligibility criteria were encouraged to participate. However, questionnaires were administered to only those who agreed to participate and these volunteers constituted the total enumeration.

Instrument for data collection

A structured interviewer-administered questionnaire was developed specifically for this study in order to collect the data from respondents. Psychological constructs were measured using scaled self-report measures adopted from previous research using the PRECEDE model and Hill-Born compliance scale for medicationadherence and appointment keeping behaviour (Kim, Hill, Born and Levine, 2000; Ajzen, 2002; Atulomah, 2014).

Measures Variables for the study were conceptualized and derived from the PRECEDE model (Green and Kreuter, 2005). The conceptual framework afforded the opportunity to select measures including outcome variables (Selfreported medication adherence and Appointment keeping, sputum smear & culture results and HIV status), independent variables (Enabling, and Reinforcing factors of the PRECEDE model) and demographic variables. These variables were incorporated into the instruments for measurement of the impact and outcome as stated in the objectives for the study.

Outcome Variables Adherence: Self-reported medication adherence (SRMA) was measured in the section C of the questionnaire with 5 questions asked about "frequency of forgetting to take prescribed medications", "frequency of deciding not to take medications for the treatment of DRTB", "frequency of stopping medication because of side effects", "too busy to take medication" and "frequency of getting refill prescription when medications runs out" measured on a 15-point four response Likert scale ranging from 'None of the time' to 'all of the time'. (1 = none of the time, 2 = some of the time,3 = Most of the time, 4 = All of the time). Similarly, two questionnaire items were used to measure Appointment Keeping (AK), the second outcome variable for adherence, on a 6-point four response Likert-type scale (1 = none of the time, 2 = some of the time, 3 = Most of the time, 4 = All of the time): "frequency of forgetting to go for an appointment", and "too busy to meet scheduled appointment with healthcare giver". AFB sputum smear and culture results and HIV status were measured on a 3-point scale to validate adherence.

Independent Variables Reinforcing factors: The role played by family member and health care provider in meeting social support need of the respondents in terms of emotional support and appraisal support and reminders to take medication was measured using the 4-response option Likert scale (1 = Strongly Disagree, 2 =Disagree, 3 = Agree and 4 = Strongly Agree), where low value represents little or no support. Aggregating the three items in the sub-scale to create a 9-point reference scale of measurement on which the respondents will be able to report the extent to which they received such support from at least a member of the family or health care provider.

Enabling Factors: This includes role played by the Government, not-for-profit organizations and family members in providing some form of tangible support such as finances for feeding and transportation, access to free drugs, free lab investigations to enable the patient cope with the challenges encountered during the DRTB treatment. These indices were measured using the 4-response option Likert scale (1 = Strongly)Disagree, 2 = Disagree, 3 = Agree and 4 =Strongly Agree), where low value represents little or no support. Aggregating the three items in the sub-scale created a 9-point reference scale of measurement on which the respondents will be able to report the extent to which they received such support from at least a member of the family, the Government or health care provider.

The content and face validity were assessed and pre-tested before the actual data collection. The instrument was filled by face-to-face interview with DRTB patients facilitated by trained research assistants attending to these patients during monthly OPD visit.

Data analysis and management

Descriptive Statistics such as frequency distributions, means, standard error of mean (SEM) and standard deviation (SD) were used to summarize and evaluate socio demographics, social/environmental factors including reinforcing and enabling factors and medication adherence behaviour. Data collected from respondents using the administered questionnaire were reviewed for completeness, edited and coded. The responses were fed into the SPSS software and double checked to ensure accuracy. Survey responses were treated with utmost confidentiality. Data analysis was performed using IBM Statistical Package of Social sciences SPSS 22 version (Inc. Chicago, IL, USA). Regression analysis was conducted to validate the association between independent variables and medication adherence behaviour. The level of significance was set at $P \le 0.05$ for all statistical procedures.

Ethical issues/considerations

Ethical clearance was obtained from the Health research and ethic committee in each state and informed consent was obtained from the participants before recruiting them for the study.

Results

Demographic characteristics of participants

A total of 300 questionnaires were administered to participants with 88.7% (266) response rate. In this study, the majority (16.5%) of the respondents were between 38–42 years of age and there were more males (61.3%). Most of the participants (89.2%) had formal education at primary school (14.7%), secondary school (44.4%), post-secondary (15.4%) and University (14.7%) levels.

Majority of the participants reported were selfemployed (46.2%). Almost three-quarter (74.1%) of the respondents were Yoruba by ethnicity. (*See Table 1*).

Measures of Social Determinants and Treatment Adherence involved in DRTB Treatment Adherence among Participants in this Study

Social and Environmental Factors The study considered certain Reinforcing and Enabling factors such as providing emotional support, reminders to take medication, appraisal support and tangible support as the Social and Environmental factors influencing adherence in drug resistant TB treatment. Results recorded for reinforcing factors measured on a 9-point reference scale was a mean of 6.45 (0.11) and SD of 1.87. Similarly results recorded for enabling factors measured on a 9-point reference scale gave a mean score of 6.41(0.12) and SD of 1.91. (See *Table 2*).

Outcome Measures for Medication Adherence and Appointment-Keeping The level of Treatment Adherence (SRMA) as a primary outcome in DR-TB treatment among the participants was measured on a 24-point reference scale. Measure of Self-Reported Medication Adherence (SRMA) on 18-point reference scale was 15.47 \pm d 2.67 translated to a prevalence of 85.9%. Similarly, results recorded for Self-Reported Appointment-keeping measured on 6point rating scale was 4.86 \pm 1.45. (See Table 2).

Linear regression

The result of covariate analysis characterizing the relationship between Reinforcing factors and enabling factor as defined by the conceptual framework showed significant relationship (p<0.01). Likewise, Medication adherence was dependent on Social/Environmental factors at 0.01 level of significance.

Binary logistic regression

Binary logistic regression was conducted to identify predictors associated with medication adherence in drug resistant TB patients. Enabling factors with OR=1.44, (95% CI=1.078-1.919, p=0.013) predicted treatment-adherence most significantly. The odd ratio (OR) indicates that Enabling factor is about 1.4 times more significant in predicting treatment-adherence for participants in this study. Likewise, a combination of Enabling and Reinforcing factors as social/Environmental factors with OR=1.27, (95% CI=1.049-1.535, p=0.014) similarly predicted treatment-adherence in patients (*See Table 3*).

Variables	Frequency Percent N (%)		
Gender:			
Males	163	61.3	
Females	103	38.7	
Ethnicity:			
Yoruba	197	74.1	
Igbo	33	12.4	
Hausa	16	6.0	
Others	20	7.5	
Education:			
Non-Formal	28	10.5	
Primary	39	14.7	
Secondary	118	44.4	
Post-Secondary	41	15.4	
University	39	14.7	
Occupation:			
Civil Servant	17	6.4	
Self-Employed	123	46.2	
Trader	49	18.4	
Professional	24	9.0	
Housewife	7	2.6	
Retired	11	4.1	
Student	34	12.8	
Clinical Features			
Sputum Result Neg	237	89.1	
Culture Result Neg	207	77.8	
HIV Status Neg	246	92.5	

Table 1. Demographic characteristics of participants in the study

Variables	Reference Scale of	N=266		Dravalance (0/)	
v ariables	Measure	$\overline{X}(SE)$	±SD	Frevalence (%)	
Social/Environmental Factors	18	12.86(0.18)	2.99	71.44	
 Reinforcing Factors 	9	6.45(0.11)	1.87	71.67	
 Enabling Factors 	9	6.41(0.12)	1.91	71.22	
Treatment-Adherence	24	20.34(0.21)	3.37	84.75	
Medication Adherence	18	15.47(0.16)	2.67	85.94	
• Appointment-Keeping	6	4.86(0.09)	1.45	81.00	

 Table 2. Social Determinants and Treatment Adherence involved in DRTB Treatment Adherence among

 Participants in this Study



Figure 1. Correlation analysis of variables measured

Table 3. Logistic regression analysis of factors associated with medication adherence in DR-TB patients

Variables	В	SE	Wald	OR	95%CI	p-value
Gender	0.515	0.709	0.528	1.67	0.417-6.714	0.468
Reinforcing	0.233	0.160	2.127	1.17	0.923-1.725	0.145
Enabling	0.364	0.147	6.118	1.44	1.078-1.919	0.013**
Social/Environment	0.238	0.097	6.036	1.27	1.049-1.535	0.014**

Discussion

The study explored all social and environmental factors (reinforcing and enabling factors) defined by the PRECEDE conceptual model including demographic characteristics of participants in this study. Findings revealed that there were more males (61.3%) in this study which is in line with other studies (Johnson et al, 2015). In most low and middle-income countries, about two-thirds of reported TB cases are men and only one-third women. A report from a workshop on the role of gender in tuberculosis infectivity

concluded that a combination of biological and social factors accounted for the observed differences in prevalence (Diwan *et al.*, 1998). The large difference in the proportion of men to women could also be attributed to smoking found in men more than in women. Trends reported from 2000 to 2016 revealed that 6% of women smoked, compared to 35% of men (Ritchie, 2019). Other possible explanations for the high male-to female ratio may be the higher share of TB cases among men which is consistent with evidence from prevalence survey. (WHO Global TB report, 2019).

Fair adherence was observed in this study in which 84.52% of participants were able to adhere to DR-TB treatment out of 266 DR-TB patients who took part in the study. No operational and standardized definition of adherence to anti-TB treatment is currently available in literature. However, for most chronic diseases, greater than 80% adherence is considered successful. A frequently used definition of non-adherence is the WHO-recommended measure, which defines a TB treatment defaulter as a patient who interrupted treatment for 2 consecutive months or more, but some studies considered a patient who had missed 10% or more of the total prescribed doses of TB drugs as non-adherent (W.H.O, 2014; O'Donell et al., 2014). Other studies have defined adherence as attending all clinic visits, taking at least 70-90% of prescribed doses or better still taking all doses (W.H.O, 2014; Valencia et al., 2016).

The study also evaluated components of Social and Environmental factors that impacts on treatment adherence in drug resistant TB patients. These factors were the reinforcing and enabling factors that are relevant for adherence to treatment among DR-TB patients in south-west Nigeria. In many developing countries including Nigeria, poorly functioning general health systems contribute to poor TB diagnosis and treatment outcomes that may lead to the development and spread of drug resistant TB. This study revealed that enabling factors such as free drug supplies and transportation support to meet all clinic appointments and monthly follow up by health care workers as well as access to necessary lab investigations were predictors of good adherence in patients on second line drug resistant TB treatment.

Effective organisation of service delivery, adequate and motivated health workforce, regular and uninterrupted drug supply, access to rapid diagnostic tests are enabling factors known to improve TB treatment outcome. A study conducted in four European countries including Austria, Bulgaria, Spain and the United Kingdom revealed the following health care system factors as key to achieving good treatment outcomes for patients with multi-drug resistant tuberculosis patients: timely diagnosis of DR-TB, financial systems that ensure access to full course of treatment and support for MDR-TB patients, patient centred approaches with strong intersectoral collaboration that address patients emotional and social needs and dedicated health care workers who are able to provide the needed supports for patients (De Vries *et al.*, 2017).

On the other hand, reinforcing factors such as social, emotional and appraisal support from family members and health care workers did not significantly predict treatment adherence in this study. However, reinforcing factors were found to be positively correlated with enabling factors which ultimately predicted adherence in this study. In a qualitative study conducted in Eritrea, lack of social support for most of the patients was an importance barrier to adherence as were stigma, medication side effects and long treatment duration. Recognized as an enabler to treatment adherence, health workers had good communication and positive attitude towards their patients (Gebreweld et al., 2018). It is popularly known that people infected with TB are often stigmatised by the community and as a result suffer from depression and suicidal thoughts which may lead to substance abuse. This may be compounded by the complexity of regimen and the long duration of treatment. They may encounter financial problems, discrimination and are generally afraid to disclose their diseases to others to avoid embarrassment or being stigmatised. The provision of social support from family member, health care workers, treatment supporters and the wider community plays a distinct role in affecting patients' psychosocial wellbeing.

Social support refers to a person's perception and confirmation that he/she is part of a social network of mutual obligations that loves and cares for him, while holding him in high esteem (Cobb, 1976). Social support is determined by access to informational, four resources: emotional, companionship and material supports. A large body of evidence has shown that social support is a predictor of health status and mortality and is key in influencing health-seeking behaviours, treatment adherence, and health outcomes (Van Hoorn et al., 2016; Yin et al., 2018; Bhatt et al., 2019). Hence, Social support interventions in patients with TB were recommended by W.H.O for the programmatic management of drug resistant TB and the new End TB strategy (WHO, 2014).

Limitations

One of the main limitations of our study is the selection bias, as the patients were recruited from

the monthly out -patient DR-TB clinic in the TB unit, thus we may expect that all patients who voluntarily decided to attend were also the most adherent. Patient recall bias and other information biases also limits reliability of self-reporting, an indirect method as a tool for measuring adherence. Despite these limitations, the low cost and relative simplicity of these methods contributes to their popularity. Also, they can be applied to any treatment period but do not provide conclusive measurement of adherence. Self-report and healthcare professional assessments are the most common tools used to rate adherence to medication (Velligan et al., 2007). The most common drawback is that patients tend to underreport non-adherence to avoid disapproval from their healthcare providers (Vik et al., 2004).

Conclusion

Current treatment regimens for TB disease require combinations of multiple drugs for several months, resulting in a global cure rate of 85% for DS-TB, 56% for multidrug-resistant TB (MDR-TB) and 39% for extensively drug-resistant TB (XDR-TB) (WHO Global TB report, 2019). The main challenges in treatment of TB disease are the duration and complexity of treatment regimens, difficulties in adherence, toxic side-effects, drug resistance and the absence or limited availability of paediatric drug formulations for second-line treatment (WHO Global TB strategy, 2019). The PRECEDE Meta-model deployed in this study provided us with a comprehensive behaviour theory-based approach to improve medication adherence in drug resistant TB patients in Nigeria. The model indicated that social/environmental factors (enabling) such as access to free drugs, transportation supports and monitoring of lab indices by health care worker involved in medication adherence and appointment-keeping were both predictors of improved adherence and treatment outcomes in drug resistant TB patients. Patients' level of treatment-adherence was fair.

However, a number of lessons have been learned which includes the use of, theory-guided programs to influence health behaviour, including health promotion and health education programs and interventions which are beneficial to participants and communities. Special attention should be given to enabling and reinforcing factors during patient education through social learning and structural support, which the study identified as inadequate, to optimize treatmentadherence in DR-TB patients.

Conflict of interests

The authors declare no conflict of interests regarding the publication of this paper.

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