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RESEARCH ARTICLE

Factors Associated with Default from TB Treatment Among Tuberculosis Patients in BUSIA Country

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Abstract

Tuberculosis remains a major health problem in many tropical countries, including Kenya. Defaulting from treatment has been an obstacle to treatment management control. Inability to complete the prescribed regimen is quite common in self-administered treatment and an important cause for treatment failure, relapses, acquired drug resistance and on-going transmission of infection. The objective was to determine factors associated with default from TB treatment in Busia County. A Cross-sectional descriptive study was conducted on 249 patients; sequential enrolment was conducted of TB patients collecting drugs within Busia County. The data was then converted to Stata 13 for futher analysis. Descriptive statistics was used in the form of frequencies, tables, charts and graphs. To assess the association, Chi-square tests (χ^2) , t-test (for numerical variables) was used. Association was further tested using regression models; I carried out a univariate analysis on all the indicator variables and checked for statistical significance at 95% confidence intervals. Out of 249 study participants, 17 % (42) were defaulters and 83 % (207) were non defaulters and males were 61% (152) while females were 39% (98). The characteristics that were statistically significant were history of alcohol consumption (OR 3.20; 95% CI 1.50 to 6.84 and P value 0.003), history and quantity of cigarette smoking (OR 3.20; 95% CI 1.50 to 6.84 and P value 0.001),vomiting (OR 2.07; 95% CI 1.06 to 4.06 and P value 0.033) and nausea (OR 1.99; 95% CI 1.01 to 3.89 and P value 0.046) as side effects experienced during taking TB drugs and taking TB drugs before meals (OR 1.99; 95% CI 1.01 to 3.89 and P value 0.043). Adherence to TB treatment in Busia County is a behavioral issue involving patient factors; alcohol intake, health care poor attitude and cigarette smoking that were most cited reasons for default, side effects were also cited to be a reason for defaulting like vomiting and nausea. Measures on patient behavioral indicators and maintenance of an effective communication channel between health facilities and patients during the treatment more focus on healthcare motivation, training and track patients on their intensive phase of treatment is recommended.

Background Information

Tuberculosis (TB) is an airborne bacterial disease. The causal agents are Mycobacterium Tuberculosis, and occasionally Mycobacterium Bovis and Mycobacterium African [1]. Mycobacterium TB infects a third of the world's population, roughly two billion people [1]. In 2013 an estimated 1.8 million people died from TB, and approximately 9.4 million new cases were diagnosed, of which the majority were in Asia and Africa [1]. TB remains a major health problem in many tropical countries, including Kenya. Defaulting from treatment has been one of the major obstacles to treatment management and an important challenge for TB control. Inability to complete the prescribed regimen which is quite common in self-administered treatment is an important cause for treatment failure, relapses, acquired drug resistance and on-going transmission of infection [2].

Kenya subscribes to the internationally accepted World Health Organization (WHO) strategy in TB control and treatment that is tailored from WHO recommended regimes. Although treatment duration for TB in

Kenya was previously 8 months, a 6-months regime was started in 2009.The first two months of treatment (intensive phase)-a combination dose of isoniazid, rifampicin, pyrazinamide and ethambutol (2RHZE) is used daily followed by 6 months of ethambutol and isoniazid (6EH) or 4 months of rifampicin and isoniazid (4RH) for new patients. To be effective, however, the drugs must be taken exactly as prescribed [3].

Non-adherence to TB treatment has serious negative consequences, not only for individual patients and their families, but also for societies, in the form of Multidrug-resistant TB (MDR) which is much more difficult and expensive to treat. During the intensive phase of treatment, patients collect drugs from facilities weekly while monthly collections are done during the continuation phase. The treatment regime for retreatment patients is 8 months and includes Streptomycin (S) in the first 2 months. [3].

There were 8.7 million range (8.3-9.0 million) incident cases in 2011 including 1.1 cases among PLHIVs. Over the same year 6.2 million notified cases of TB against an estimated 8.7 million cases, representing a case detection rate (CDR) of 66% [3].

Kenya is ranked 15th among the 22 high TB burden countries that account for 80% of the global TB burden and 5th in Africa. In 2012, the country notified a total of 103,159 TB cases (all forms of tuberculosis) of whom 39% were also HIV infected. Tuberculosis treatment results for TB patients started on treatment in 2013 showed a treatment success of 87% for new smear-positive pulmonary TB cases [2].

WHO Global TB Report 2013 strategy includes the four key pillars, namely: detection of smear-positive pulmonary TB in patients using sputum microscopy; directly-observed treatment with short course chemotherapy; guaranteed continuous drug supply; and a case recording system tracking treatment outcomes by a health worker or other responsible persons, including household members or others with whom the patient has a close relationship, at least during the intensive phase of treatment. Some patients fail to adhere to treatment and eventually default before completing the course [4]. Patients, whose treatment is interrupted for 2 consecutive months or more, as defined by W.H.O, are reported as 'Out of Control' at the end of treatment period.

Poor adherence to treatment means that patients remain infectious for longer and are more likely to relapse or succumb to tuberculosis. Treatment default is a serious problem in tuberculosis control. It may lead to persistence of infectious source, increased mortality, increased relapse rates, and facilitate the development of resistant strains. Erratic or selective compliance to treatment and default could result in treatment failure, foster emergence of drug resistant tuberculosis and may increase the cost of treatment. Due to serious consequences of default, National TB Programs offer social support to ensure treatment compliance and completion to maximize the likelihood of cure, hence avoid adverse treatment outcomes and minimize the chances of developing drug resistance [5].

Several important factors have contributed to the drug-resistant TB epidemic, Busia County with defaulter rate of 7.0%, has had high treatment default rates amongst other Counties' in Kenya that resulted in the creation of large numbers of MDR TB strains, the recent exponential rise in MDR TB cases which is a major cause of mortality posing a greater challenge to effective control of this disease. Its management and treatment is very difficult and expensive thus overstretching the already strained resources for TB control in most developing countries.

Problem Statement

Mycobacterium Tuberculosis infects a third of the world's population, roughly two billion people (Young, Strasser, & State, 2012). In 2008 an estimated 1.8 million people died from Tuberculosis, and approximately 9.4 million new cases were diagnosed, of which the majority were in Asia and Africa (Norgbe, G K, J.E. Smith, 2011). In 2010, 8.8 million people fell ill with Tuberculosis globally, and a total of 1.4 millionpeople died as a result of the disease, most of these cases and deaths (about 95%) occurring in developing countries [3]. The disease, which

affects both adults and children, remains a major cause of mortality despite availability of effective treatment [6]. The government of Kenya policy provides for free Tuberculosis treatment that includes consultation at clinics, laboratory services and non-payment for drugs [7]. Close to 7% of patients on tuberculosis treatment in Busia County defaulted from therapy in 2013 in spite of free Tuberculosis services offered by the government [7]. A patient who default from treatment, promote development and transmission of multi-drug resistant tuberculosis (MDR-TB) and treatment failure (Pablos et al., 1998). Multi drug-resistant strains of Tuberculosis and Extreme Drug-Resistance in Tuberculosis (XDR- TB) are currently emerging as major global public health concerns [8]. Treatment of multi drug-resistant tuberculosis requires a prolonged duration of over two years and use of expensive second-line drugs not easily available in most countries [2]. Despite the 7% default rate of Tuberculosis treatment in Busia County, factors associated with default from treatment are poorly understood.

Methodology

Study Design

Cross sectional descriptive study design was used. The study followed a quantitative approach, subjects on TB treatment between April-September 2015 were considered in the study to determine factors associated with default from TB treatment. The respondents' knowledge and understanding of TB and treatment, as well as their reasons for defaulting from treatment were described. Patient's experiences on TB treatment were described within the study period.

Study Population

In this study, the populations comprised patients diagnosed with Tuberculosis and are on treatment between months of April to September 2015 in Busia County. Study was carried out in the following hospitals; Busia County Referral Hospital, Khunyangu, Nangina, Alupe, Port victoria, Bumala A and Kocholia. No sampling was done as Tuberculosis patients in their continuation phase of treatment were considered in the study. The study involved a population of 243 subjects.

Sample Size Estimation

Study design was a cross sectional descriptive study that enabled to determine factors associated with default from TB treatment in Busia County. Quantitative method was employed through questionnaire administration and to asses if socio-economic factors can predict TB treatment outcome. Convenience sampling was employed to obtain a total of 243 subjects. A 95% confidence interval was used.

Sampling Procedures

From the purposively sampled facilities, Tuberculosis patients in their continuation phase between April and September 2015were enrolled. To obtain 243 subjects, sequential enrolment of TB patients collecting drugs in their assigned facilities were considered. The subjects were contacted during working hours (8 am to 5 pm) and this was done in facilities where they are collecting TB drugs.

Data Collection Procedure

Research assistants conducted interviews to TB patients enrolled for treatment. Explanation was done to subjects about the aim and benefits of the study, consent was obtained and questionnaire administered, the questionnaire was also interpreted to the subjects. However, those respondents who were in a position to interpret the questions (either in English or Kiswahili) were asked to complete the questionnaires themselves. Questionnaire was administered either in English or Kiswahili and data collection lasted for three weeks and interviews administered lasted for an average of 30 minutes.

Data Management and Analysis

All completed questionnaires were verified for accuracy and consistency. Data was entered in SPSS IBM Version 20 and backed up in a computer and a thumb drive. The data was then converted to Stata 13 for futher analysis. Descriptive statistics was used in the form of frequencies, tables, charts and graphs. To assess the association, Chi-square tests (χ^2) , t-test (for numerical variables) was used. Association was further tested using regression models; Logistic regression to investigate the factors associated with treatment defaulting was carried out. We carried out a univariate analysis on all the indicator variables and

checked for statistical significance at 95% confidence intervals. Those variables that had a p value of at least 0.15 were futher included in the multivariate model where we carried out a stepwise backwards elimination until only the significant variables were left in the final model.

Ethical Approval

The study was submitted for approval to the Jaramogi Oginga Odinga Teaching and Referral Hospital Ethics Review Committee and forwarded to the Busia County Administration. Clearance was sought from Hospital administration. The study was well explained to all the participants, those who consent were requested to sign the consent form (Appendix 3 in English or Appendix 5 the Swahili translated). Confidentiality was maintained throughout.

Results

Characteristics of Study Population

In this study, a total of 249 participants were enrolled between April and September 2015, Out of study participants, 17 % (42) were defaulters and 83 % (207) were non defaulters and male participants were 61% (152) while females were 39% (98). The ages of the respondents ranged from 15 to 65 years, with the age between 25-34 years being the largest 37 % (n = 91), followed by 35-44 years with 25% (n=63) **Figure 1.**

As regards to the number of day's study participants defaulted, 29% defaulted for 1-2 months and about 10% defaulted for 5-6 months Figure 2.

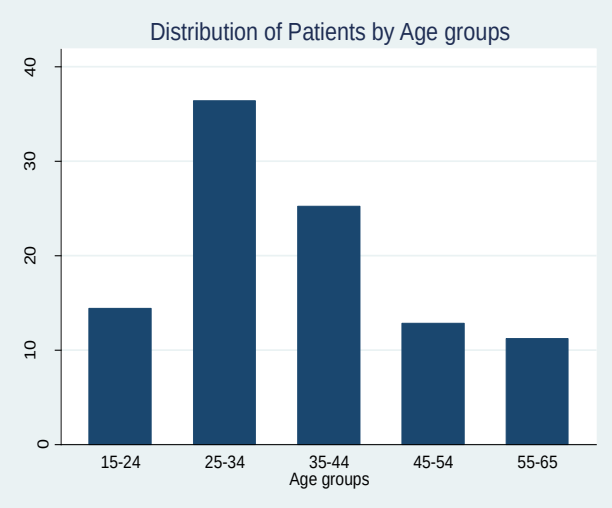

Figure 1: Distribution of patients by age groups

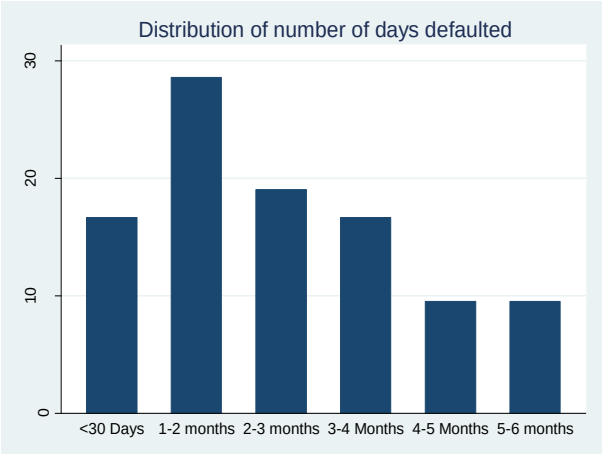

Figure 2: Distribution of number of days in month's patients defaulted on TB drugs

The main reason for defaulting amongst TB patients was being occupied due to employment or working at 26%, followed by mistaking that they had already finished treatment at 21% and being ashamed of coming to the hospital for treatment at 1

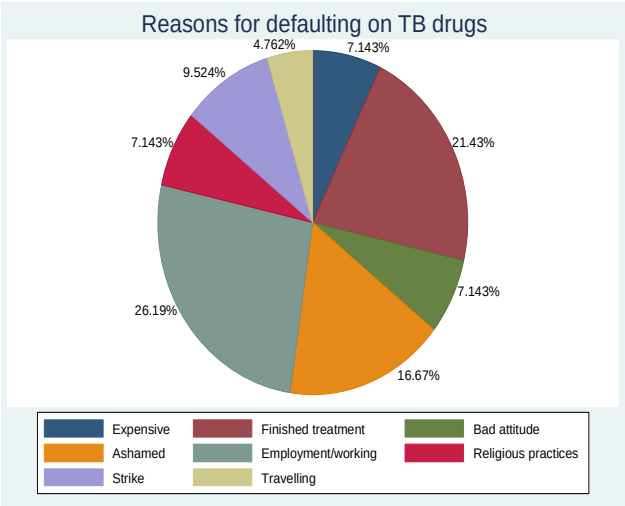

Figure 3: Reasons for defaulting on TB drugs

Socio-Demographic Factors

In bivariate analysis we compared the socio-demographic characteristics by defaulter status; among the defaulters, there were more males compared to females, of the males, 67 % (n = 28) were defaulters and 59 % (n = 123) were non-defaulters, while of the females, 33 % (n = 14) were defaulters and 41 % (n = 84) were non-defaulters. Age group 24-34 years was prone to defaulting compared to other age groups and educational level below primary was associated with defaulting, however, these differences were not statistically significant.

There was no statistical difference in the defaulters versus non defaulters when we compared by socio demographic characteristics.

Table 1: Characteristics of Socio-demographic factors by default status

Characteristics		Non-Defaulters N=207 (83%) n (%)	Defaulters N=42 (17%) n (%)	P value
Gender	Male	123 (59.4)	28 (66.7)	0.381
	Female	84 (40.6)	14 (33.3)	
Age (Years)	15-24	32 (15.5)	4 (9.5)	0.817
	25-34	75 (36.2)	16 (38.1)	
	35-44	52 (25.1)	11 (26.2)	
	45-54	25 (12.1)	7 (16.7)	
	55-65	23 (11.1)	4 (9.52)	
Marital status	Single	42 (20.3)	9 (21.4)	0.600
	Married	122 (58.9)	23 (54.8)	
	Widowed	21 (10.1)	7 (16.7)	
	Divorced/ Separated	22 (10.6)	3 (7.1)	
Educational Level	None	39 (19.1)	9 (21.4)	0.133
	Primary	124 (60.8)	25 (59.5)	
	Secondary	38 (18.6)	5 (11.9)	
	Tertiary	3 (1.5)	3 (7.1)	

Table 2:Univariate analysis of determinants of drug defaulting on Socio-demographic factors

Characteristics		OR (95% CI)	P value
Gender	Male	1	
	Female	0.73 (0.36 – 1.47)	0.383
Age (Yrs)	15-24	1	
	25-34	1.71 (0.53 – 5.51)	0.371
	35-44	1.69 (0.50 – 5.77)	0.400
	45-54	2.24 (0.59 – 8.51)	0.236
	55-65	1.39 (0.31 – 6.15)	0.663
Marital status	Single	1	
	Married	0.88 (0.38 – 2.05)	0.767
	Widowed	1.56 (0.51 – 4.76)	0.439
	Divorced/ Separated	0.64 (0.16 – 2.59)	0.528
Educational Level	None	1	
	Primary	0.87(0.376-2.029)	0.753
	Secondary	0.57 (0.175-1.857)	0.351
	Tertiary	4.33 (0.748-25.10)	0.102

Patient Related Factors

There was a notable statistical difference for defaulter's verses non defaulters when we investigated patient related factors. The characteristics that were statistically significant were history of alcohol consumption (OR 3.20; 95% CI1.50 to 6.84 and P value 0.003), history and quantity of cigarette smoking (OR 3.20; 95% CI 1.50 to 6.84 and P value 0.001),vomiting (OR 2.07; 95% CI 1.06 to 4.06 and P value 0.033) and nausea (OR 1.99; 95% CI 1.01 to 3.89 and P value 0.046) as side effects experienced during taking TB drugs and taking TB drugs before meals (OR 1.99; 95% CI 1.01 to 3.89 and P value 0.043) as shown in Table 3.

Table 3: Univariate analysis of determinants of drug defaulting on patient related factors.

Characteristics		OR (95% CI)	P value
Ever taken alcohol	No	1	
	Yes	1.99 (0.96 – 4.11)	0.065
Take alcohol currently	Past six months	1	
	Currently taking	3.20 (1.50 – 6.84)	0.003
Does alcohol affect drug intake	No	1	
	Yes	2.36 (0.75-7.37	0.140
Time of alcohol intake	Daily	1	
	Occasionally	0.15 (0.05-0.49)	0.002
	Never	0.10 (0.03-0.35)	0.000
Ever smoked	No	1	

	Yes	3.77 (1.87 – 7.63)	<0.001
Currently smoking	No	1	
	Yes	6.62 (2.25 – 19.45)	0.001
Number of cigarettes per day	<6	1	
	6-12	1	
	12-24	3 (0.12-73.64)	0.501
Vomiting	No	1	
	Yes	2.07 (1.06-4.06)	0.033
Nausea	No	1	
	Yes	1.99 (1.01 – 3.89)	0.046
Meals before drugs	No	1	
	Yes	2.01 (1.02-3.95)	0.043

Healthcare Factors

Among the healthcare related factors, the healthcare worker attitude was a significant factor for defaulting in that poor healthcare worker attitude attributed to 7 %(3) compared to non-defaulters 1% (2). Healthcare worker was associated to default from TB treatment (**OR 7.10 CI 1.13 to 44.62** and **P value 0.037) Table 4**.

Table 4: Univariate analysis of determinants of drug defaulting on Healthcare related factors

Characteristics		OR (95 % CI)	P value
Clinic hours convenient	No	1	
	Yes	0.93 (0.33-2.60)	0.886
Time taken to collect drugs at clinic	<1 hour	1	
	>1 hour	1.56 (0.76-3.19)	0.224
Health worker attitude	Good	1	
	Fair	0.71 (0.34 – 1.49)	0.363
	Poor	7.10 (1.13 – 44.62)	0.037
Told why TB treatment takes 6 months	No	1	
	Yes	5.41 (0.71-41.12)	0.103
TB transmission mode	Aerosols	1	
	Sexual intercourse	-	
	Don't know	1.03 (0.40 – 2.68)	0.944

Table 5: Multivariate analysis of determinants of drug defaulting

Characteristics		OR (95% CI)	P value
Ashamed of taking drugs	No	1	
	Yes	2.14 (0.99 – 4.66)	0.054
Currently smoking	No	1	
	Yes	3.87 (1.15 – 13.07)	0.029
Take alcohol currently	No	1	1
	Yes	2.67 (1.15 – 6.18)	0.022
Health worker attitude	Good	1	
	Fair	0.71 (0.34 – 1.49)	0.363
	Poor	7.10 (1.13 – 44.62)	0.037

Factors FOR Default

Finally to check for factors associated with defaulting, we carried out a multivariate analysis after carrying out a backwards stepwise regression. The factors that were associated with defaulting, were shame of taking drugs (OR=2.14; 95% CI 0.99-4.66), currently smoking within the last six months (OR=3.87; 95% CI 1.15-13.07), currently taking alcohol (OR=2.67; 95% CI 1.15-6.18), while poor health worker attitude contributed to defaulting more, where the odds of defaulting for those who experienced poor attitude being 6.96 compared to those who experienced good healthcare worker attitude (OR=6.96; 95% CI 1.00-50.70) as shown in Table 5.

Discussion

Taking into account the long duration of anti-tuberculosis treatment and rapid response after initial phase, the authors were quite concerned about the socio demographic factors, patient related factors and healthcare factors of the study participant regarding TB treatment duration.

Defaulting early during treatment period may be due to behavioral factors, inadequate patient pre-treatment counseling, unimproved pre-treatment health education, poor training and motivation of healthcare personnel , these is likely to lead to adverse outcomes (treatment failure, drug resistance and death).

Socio Demographic Factors

Male gender and education level of the TB patients was found to be strongly associated with the default rate, in this study, education level was dichotomized in four. Patients with education level of at least primary are found having a higher chance of defaulting **25 (59.5%)** compared with those having education level above secondary level **5 (11.9%).** This finding is also being supported by other studies in the study hypothesis and coherent with several literatures such as the study which conducted in Kassala state, Nairobi where they found out educational level below primary is highly associated with defaulting [9,10]. Males have a higher chance of defaulting from TB treatment compared to females 28 (66.7%) this agrees with study done in Ghana Sudan and Nairobi and where they found male gender defaulting from treatment Of the males, 43.5% (n = 30) were defaulters and 56.5% (n = 39) were non-defaulters, while of the females, 31.1% (n = 19) were defaulters, response rate was 98%. 182 (60.5%) of participants were males and 119 (39.5%) were females the male gender (OR 1.29; 95% CI 1.08-1.55) respectively, [1,9,10].

Tuberculosis is historically associated with poverty [11]. Other studies have linked the socioeconomically disadvantaged such as low-income earners, alcohol users and the less educated with an increased risk of defaulting from treatment [12]. This was evident from findings in this study, alcohol use was found to be independently associated with default in this study. Besides, alcohol is injurious to the liver, this potentiating the hepatic effects of anti-tuberculosis drugs.

Patient Related Factors

History of alcohol intake was cited as cause to default from TB treatment, though other studies in Nairobi and Ghana [1, 10] only based on whether the participant was either taking or not taking alcohol, our study was different in that we did further find out the history of taking alcohol and the duration of taking, participants currently taking alcohol (OR=2.67; 95% CI 1.15-6.18), were most likely to default from treatment than those who taken alcohol for the past 6 months.

Though study done in Urban setting-Nairobi [10] indicated alcohol use (OR 4.97; 95% CI 1.56-15.9) as a major factor for defaulting, same results has been indicated in our study though the odds ratio being slightly low compared to the Nairobi study. (OR 2.36 CI 0.75-7.37).My study was in a rural set up though slightly comparable with the urban setting study and the highest odds ratio as indicated above this could be due to lifestyle experienced in urban setting and the knowledge that most people living in urban setting have money and can afford buying alcohol and the congestion experienced thus enhancing high default rate.

Participants infected with HIV/AIDS 27(64.3% are highly associated with TB defaulting than those on TB treatment without HIV/AIDS 107 (51.7%). The side-

effects profile of TB chemotherapy is magnified in patients with concurrent HIV treatment [13]. Besides, combining ARV and TB drugs means taking many tablets daily and can be very difficult and challenging to a patient. Poorer TB treatment success rate for HIV positive patients has previously been reported in Busia among re-treatment patients [13].

Our study results indicate default from treatment in Busia County occurs most frequently duringthe first and second month of treatment, (29% defaulted by the end of the second month.)

Similar findings have been reported from studies among Kenyans (urban setting) and in Kassala state, Sudan 2013 [10] although, contrary, patients in South Eastern Nigeria were found to default more frequently during the continuation phase [8].

Stigma was attributed to default, similar to past findings [10] and was significantly associated with default on univariate analysis in this study .There is clear evidence of the effect on adherence by culturally influenced and attitudes beliefs about tuberculosis and its treatment. Religious and cultural factors are associated with misinformation about the medical aspects of the disease and stigmatization of persons with tuberculosis. Within the communities of the study population, 35 (85.4%) of patients indicated tuberculosis is transmitted through aerosols while 6 (14.6%) perceived they don't know how TB is transmitted.

Cigarette smoking was strongly associated with default from TB treatment, though there is no study that has highlighted on smocking as a factor to default, Busia being a rural setting most people can afford a cigarette in order to quench he/her urge to smoke, this enhanced to those smoking having a high chance of stopping treatment through the arousal of nervous system.

Other patient related factors were found having slight impact on TB default are side effects Vomiting (OR 2.07 95% CI 1.06 to 4.06 and P value 0.033), Nausea (OR 1.99 95% CI 1.01 to 3.89 and P value 0.046) have influence on treatment default.

Health Care Related Factors

The probability of stopping treatment after patient experienced poor healthcare attitude was seven times higher (OR 6.96 95% CI 1.00 to 50.70 and P value 0.037). This finding was observed as well in several studies such as those which were carried out in Ghana and Kenya during 2011 [6,10].

Poor healthcare attitude was cited by the highest proportion of defaulters as the main cause of defaulting, defaulters 3 (7.32%) and non-defaulters 2 (0.98%)

This was further confirmed in the study as poor healthcare attitude on patients undergoing TB treatment was found to be associated with default, similar to findings in Kassala state, Sudan [9].

Predictive Factors for default

This study showed that majority participants were not employed 27 (64.3%) and were likely to default from treatment compared to employed 12 (28.6).The results agrees with study done in Nairobi and Sudan where they found out that the unemployed group are likely to default from TB treatment [1,10].The same study found out that unemployed and those earning less than 1USD had a higher chance of stopping TB treatment, same results were echoed by my results where I found out that the unemployed 15 (35.7%) and low income earners (less than 1 USD) were also likely found to default 18 (42.9%). There was no statistical difference in the defaulters versus non defaulters when we compared the socio-economic factors [14-20].

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