DETERMINANTS OF RETREATMENT WITH FIRST LINE ANTI-TUBERCULOSIS DRUGS IN SMEAR POSITIVE PATIENTS IN ADAMAWA STATE, OCTOBER 2012 – JUNE 2013

BY

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ATTESTATION

I declare that the work in the dissertation entitled "**Determinants of Retreatment with First Line Anti-tuberculosis Drugs in Smear Positive Patients in Adamawa State**" has been performed by me in the Department of Community Medicine under the supervision of Dr. M. N. Sambo and Prof. K. Sabitu. The information derived from the literature has been duly acknowledged in the text and a list of references provided. No part of this dissertation was previously presented for another degree or diploma in any university.

Dr. MALAU, Mangai Toma	**Signature**	**Date**

CERTIFICATION

This thesis entitled "**DETERMINANTS OF RETREATMENT WITH FIRST LINE ANTI-TUBERCULOSIS DRUGS IN SMEAR POSITIVE PATIENTS IN ADAMAWA STATE**" by **Dr. MALAU, Mangai Toma** meets the regulations governing the award of the degree of Master in Public Health-Field Epidemiology of Ahmadu Bello University, and is approved for its contribution to knowledge and literary presentation.

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DEDICATION

This academic work is dedicated to my darling wife Kyagarmun Love Mangai and our son Master Fasamin. I received strength and encouragement from God through them.

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To my wife Kyagarmun and son Fasamin, parents and siblings, I value you greatly. Thank you for keeping the oneness soaring high.

SUMMARY

Retreatment is indicated in tuberculosis (TB) patients if they fail or default from initial treatment or relapse after initial treatment success. TB retreatment in Nigeria grew from 2,395 in 2002 to 8,787 in 2011. Adamawa state alone from 2002 – 2012, recorded an average of 177 retreatment cases per year. Retreated patients transmit TB including potentially drug resistant-TB, waste drugs and incur extra cost to TB Control Programme. We investigated retreatment determinants in smear positive patients, age ≥15 years, taking first line anti-TB drugs (FLADs), in Adamawa state from 4th quarter 2012 to 2nd quarter 2013.

Case-control study conducted. Cases, pulmonary TB (PTB) patients, on retreatment with FLADs, and with pretreatment smear positive result. Controls, PTB patients, with pretreatment smear positive result and converted to smear negative in 5th month while on the initial FLADs, and in whom there is no default, failure or relapse. Sociodemographic, knowledge and attitude, treatment adherence and disease severity factors obtained using pre-tested questionnaires through physical interview and data abstraction from TB registers. Data cleaned and analysed using Epi Info version 3.4.3 at 5% alpha level of significance and 95% confidence. Odds ratio (OR) used to compare association. Ethical clearance obtained from the state Research Ethics Committee (Ref.No S/MOH/1131/I/24).

Of 243 patients studied (81 cases, 162 controls), mean age 35.2 ± 11.7 years (cases 37.8 ± 10.6; controls 33.9 ± 12.0), 70.4% young adults 20 – 40 years (cases 71.6%; controls 69.8%), 69.1% males (cases 79.0%; controls 64.2%), 59.3% married (cases 56.8%; controls 60.5%), and 46.1% attained secondary education (cases 44.4%; controls 46.9%).

Determinants identified– Knowledge on causative agent based on score below its mean 80.74% [crude odds ratio (cOR) 1.98; 95% CI: 1.05-3.74] and attitude on measures to improving health while on anti-TB based on score below its mean 42.47% (cOR 1.77; 95% CI: 1.01, 3.08). Male gender (cOR 2.1; 95% CI: 1.13-3.92), unemployment (cOR 1.9; 95% CI: 1.09-3.30) and clinic location ≥5 km from residence (cOR 2.6; 95% CI: 1.12-6.16). Smoked till at least onset of treatment (cOR 2.5; 95% CI: 1.42-4.26), daily smoking ≥11 cigarettes (cOR 3.2; 95% CI: 1.29-7.75), alcohol consumption till at least onset of treatment (cOR 2.4; 95% CI: 1.39-4.29) and alcoholism (cOR 3.1; 95% CI: 1.19-7.92). Ever discriminated against (cOR 2.2; 95% CI: 1.17-4.16), ever missed clinic (cOR 2.3; 95% CI: 1.25-4.03), ever missed anti-TB doses (cOR 2.3; 95% CI: 1.28-4.08), TB/HIV comorbidity (cOR 1.95; 95% CI: 1.07-3.56), concurrent drug use (cOR 2.1; 95% CI: 1.17-3.74) and used of social support and adherence measures (cOR 0.46; 95% CI: 0.24-0.88).

Independent predictors identified were distance ≥5 km from house to clinic [adjusted odds ratio (aOR) 3.69; 95% CI: 1.38-9.90], ever smoking ≥11 cigarettes daily (aOR 3.21; 95% CI: 1.18-8.71), negative attitude on measures to improving health while on anti-TB (aOR 2.28; 95% CI: 1.15-4.52), TB/HIV comorbidity (aOR 2.49; 95% CI: 1.23-5.06) and use of social support/adherence measures (aOR 0.37; 95% CI: 0.17-0.78).

The State and Local Government Areas are recommended to site clinics closer at distances of less than 5 km from homes, introduce tobacco dependence and cessation programme in clinics, closely monitor TB-HIV comorbidity, promote healthy measures to improving health while on anti-TB and reinforce social support and other adherence measures.

Keywords: Tuberculosis, smear positive, retreatment, first line anti-tuberculosis drugs, determinants, factors.

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LIST OF ABBREVIATION AND ACRONYMS

ABU	Ahmadu Bello University Zaria
AFB	Acid Fast Bacilli
BCG	Bacillus Calmette-Guérin
CDC	United States Centres for Disease Control and Prevention
CI	Confidence Interval
DM	Diabetes mellitus
DOTS	Directly Observed Treatment Short-course
DR	Drug Resistance
DST	Drug Susceptibility (Sensitivity) Testing
E	Ethambutol
FLADs	First line anti-tuberculosis drugs
FMOH	Federal Ministry of Health
H	Isoniazid
HBC	High tuberculosis Burden Countries
HIV	Human Immunodeficiency Virus
LGA	Local Government Area
LL	Lower limit of confidence interval
MDR	Multi Drug Resistance
mg/kg	Milligram per kilogram body weight
mmol/l	Millimoles per litre
Mtb	Mycobacterium tuberculosis
MTC	Mycobacterium tuberculosis complex
NTBLCP	National Tuberculosis and Leprosy Control Programme
cOR/aOR	Crude Odds Ratio/Adjusted Odds Ratio
PHC	Primary Health Care
PTB	Pulmonary Tuberculosis
R	Rifampicin
RNA	Ribonucleic Acid
S	Streptomycin
SMOH	State Ministry of Health
TB	Tuberculosis
UL	Upper limit of confidence interval
WHO	World Health Organization
Z	Pyrazinamide

CHAPTER ONE: INTRODUCTION

1.1. Background information

Tuberculosis (TB) is a chronic infectious disease caused by any pathogenic member of *Mycobacterium tuberculosis complex (MTC).*[1,2] The most common of MTC is *Mycobacterium tuberculosis* (Mtb), first discovered by Robert Koch in March 24, 1882. Others include *Mycobacterium africanum, Mycobacterium bovis, Mycobacterium microti, Mycobacterium canettii* etc. Pulmonary tuberculosis (PTB) accounts for >80% of TB types and the common mode of transmission is by inhalation of droplet nuclei released into the environment when untreated PTB patients coughs, sneezes, spits, laughs or talks.

A person with untreated PTB is estimated, on average, to infect 10 – 15 persons annually.[3] Naturally, about 5% of persons primarily infected with Mtb will develop clinical disease within 5 years of the infection; and the other 95% will develop latent infection that may later progress to active disease[4,5] depending on agent, host and environmental factors. Overall, about 10% of infected individuals will eventually develop active TB. Overt TB, thus, could result from primary infection, reactivated latent infection, or re-infection.

TB has a wide clinical spectrum ranging from the early asymptomatic stage, the nonspecific constitutional symptoms, and specific disease-site features and to those of disease complications. However, the common clinical features of PTB include fever, weight loss, night sweats, loss of appetite and chronic cough for at least 2 – 3 weeks. Radiological and laboratory features in TB also vary depending on the site affected and immune status. Diagnosis of TB is made first on the ground of clinical acumen which is confirmed by bacteriology– culture or smear microscopy; or by newer molecular-based methods[6,7]– line probes or GeneXpert. In addition, tuberculin skin test or imaging techniques such as X-rays are required to support diagnosis.

Patients enrolled for TB treatment are grouped into new (initial treatment) and previously treated (after initial treatment) cases. Previously treated group are patients with prior history of initial intake of anti-TB drugs for ≥4 weeks and are the ones targeted for retreatment with appropriate anti-TB drugs selected based on clinical, laboratory and/or epidemiological indications. The current classification of retreatment groups **(table 1)** according to WHO are TB patients who failed or defaulted from initial treatment or relapse after initial treatment success.[8,9]

After TB is diagnosed, appropriate and full course of anti-TB drugs should be instituted immediately **(table 2 and 3)**. In the treatment of TB, the first line drugs are used in drug susceptible cases while the second line in drug resistant TB. The aims of TB treatment with the anti-TB drugs are to cure the patient, restore quality of life and productivity; prevent death from active TB or its late complications; prevent relapse of TB; reduce transmission of TB to others; and to prevent the development and transmission of drug resistance which is fast emerging.[9] In TB management, prescribers should be guided by the following key factors in their choice of anti-TB chemotherapy:

1. presence of drug-susceptible or drug-resistant TB.
2. whether the health care provider is dealing with new TB patients or previously treated TB patients– defaulters, relapsed or failed treatment.
3. whether medical history is indicative of contact with a documented multi-drug resistant (MDR) TB patient on treatment.
4. whether DR-TB is prevalent in the community as determined by MDR-TB survey.

Tuberculosis is a major cause of morbidity, disability and death globally. Approximately the world records 9 million new cases of TB, and 2 million TB deaths yearly.[10,11] In sub-Saharan region, the annual TB detection rate has quadrupled since the mid-1980s, and over two-thirds

of TB patients in the region are dually infected with HIV. It is estimated that about 200,000 deaths occur from TB/HIV comorbidity in the region. In Nigeria, the overall TB incidence rate is 311 cases per 100,000 population per year and the incidence rate for smear positive cases is 137 cases per 100,000 population per year.[12]

Documented determinants of retreatment with first line anti-TB drugs include sociodemographic factors, poor adherence to treatment protocol, severe drug side effects, disease severity and comorbidity.[13–18] The health care service providers and patients themselves influence these factors either negatively or positively. The sociodemographic factors among others are age, gender, occupation, educational and employment status, low-income level, knowledge and attitude of individuals. Others are use of psychoactive substances before, during and after treatment, patient-health worker relationship, stigma and discrimination, poor accessibility to and erratic diagnostic and treatment services in DOTS centres.[4,19] TB comorbidity with HIV, diabetes mellitus, psychiatric illness, liver pathology or chronic respiratory disease affects prognosis and increases the likelihood of TB retreatment. Concurrent use of other drugs and herbal preparations can also reduce the potency of anti-TB drugs.[18]

In Nigeria, TB treatment, prevention and control officially began in 1989 with the establishment of National TB and Leprosy Control Programme (NTBLCP). The States and Local Governments similarly established same control programme in 1991. In response to global and local challenges affecting TB control, Nigeria progressed and commenced the implementation of the WHO Directly Observed Treatment Short-course (DOTS) strategy in 1993. In a renewal of effort to fight the menace caused by TB, Nigeria in 2006, declared TB a national emergency and then adopted the new 2006 – 2015 WHO's Stop TB Strategy and the Global Plan to Stop TB.

Table 1: Patients Enrollment into the DOTS clinics[8,9]

Enrollment groups	Definition
New TB cases AFB+/-	First-timers: previously never had treatment of TB (or just taken anti-TB drugs for <1 month)
Previously treated	Previously received anti-TB drug for ≥1 month
Default	The patient whose treatment was interrupted for ≥2 consecutive months
Relapse	Cured previously from TB or completed treatment for TB and now having TB
Failure	Sputum smear or culture is positive for Mycobacterium TB at 5th month or later during treatment/MDR strains detected at any point in time of treatment, whether smear positive or negative for Acid Fast Bacilli (AFB)

+/- Stands for smear positive/negative

Table 2: Recommended doses of first line anti-TB drugs for adults[8,9]

Drug	Daily dose (range)	Daily max. dose	Thrice weekly dose (range)	Thrice weekly max. dose	Mechanism of Action	Side effects
H	5 (4 – 6)	300	10 (8 – 12)	900	Potent bactericidal that interferes with mycolic acid synthesis in replicating bacilli	•Peripheral neuropathy, hepatotoxicity neurological effects & optic neuritis
R	10 (8 – 12)	600	10 (8 – 12)	600	Potent bactericidal with a sterilizing effect in both cellular & extracellular locations. It binds to β-subunit of RNA polymerase thereby stopping transcription	•Nausea, vomiting, abdominal pains, pruritus/rash •Exfoliative dermatitis in HIV patients •Temporary oliguria, dyspnoea & haemolytic anaemia in patients taking the 3 times weekly dose
Z	25 (20 – 30)		35 (30 – 40)		Weak bactericidal with a potent sterilizing effect in a relatively acidic intracellular environment of macrophages & in areas of acute inflammation	•Hepatotoxicity •Gastrointestinal intolerance. •Hypersensitivity reactions (rare) •Hyperuricaemia •Arthralgia particularly of the shoulders
E	15 (15 – 20)		30 (25 – 35)		Inhibits arabinosyl transferase involved in bacillus cell wall biosynthesis. In combination with other anti-TB drugs prevent/delay the emergence of resistant strains	•Dose-dependent optic neuritis •Peripheral neuritis •Generalized cutaneous reaction, arthralgia & hepatotpxicity are rare
S	15 (12 – 18)		15 (12 – 18)	1000	Aminoglycoside, sensitive to Gram-negative infections. It inhibits bacterial protein synthesis	•Pains/sterile abscesses at injection sites •Cutaneous hypersensitivity reactions •Impairs cochlear functions more than vestibular part •May damage the 8th cranial (auditory) nerve causing tinnitus, ataxia, vertigo & deafness

H = Isoniazid; **R =** Rifampicin; **Z=** Pyrazinamide, **E=** Ethambutol, **S=** Streptomycin, **mg/kg** = milligrams/kilogram body weight, **max** = maximum

Table 3: Treatment regimen with first line anti-TB drugs[8,9]

Registration of groups	Intensive phase	Continuation phase	Formula presentation	Remark
New patients AFB+/-	2 month HRZE	4 month HR	Initial treatment: 2(HRZE)/4(HR)	Rule out MDR-TB when there is high suspicion
Retreatment group (previously treated patients)				
i) Default (medium to low likelihood of MDR-TB)	2 month HRZES followed by 1 month HRZE	5 month HRE	Retreatment regime: 2(HRZES)/1(HRZE) /5(HRE)	Adjust regimen appropriately after DST result
ii) Relapse (medium to low likelihood of MDR-TB)	2 month HRZES followed by 1 month HRZE	5 month HRE	Retreatment regime: 2(HRZES)/1(HRZE) /5(HRE)	Adjust regimen appropriately after DST result
iii) Failure (high likelihood of MDR-TB)	Empirical MDR-regimen 6 – 9 months	18 – 24 months		Adjust regimen appropriately after DST result

+/- Stands for smear positive/negative

H = Isoniazid; **R =** Rifampicin; **Z=** Pyrazinamide, **E=** Ethambutol, **S=** Streptomycin

1.2. Statement of the problem

TB is a major cause of morbidity, disability and death globally with the low and middle-income countries accounting for >95% of TB deaths. Data show that TB retreatment case notification in Nigeria is growing. It rose from 2,395 in 2002 to 8,787 in 2011 of which 18% treatment after default, 29% relapse, 8% treatment after failure and 45% were others.[20] In Adamawa, retreatment is a growing public issue that is stretching the already stretched health services. The

state in 2002 – 2012 on the average recorded 177 retreatment cases per year **(figure 1)**, with relapse taking the lead, followed by default and failure.[21]

The WHO Stop TB Strategy advocated that all TB patients should take their complete treatment doses without interruption. This is so because one case of retreatment can be a potential source MDR-TB to the community, which is very difficult and expensive to treat. Another consequence is the drug wastage and extra cost since the treatment is started afresh. Although the WHO 2006 – 2015 Stop TB Strategy and the Global Plan to Stop TB has helped in the overall global reduction of TB but Adamawa state is still registering high number of patients on retreatment. Documented determinants that fuel retreatment are sociodemographic, poor adherence to the drugs/follow-up, and TB severity and comorbidity.

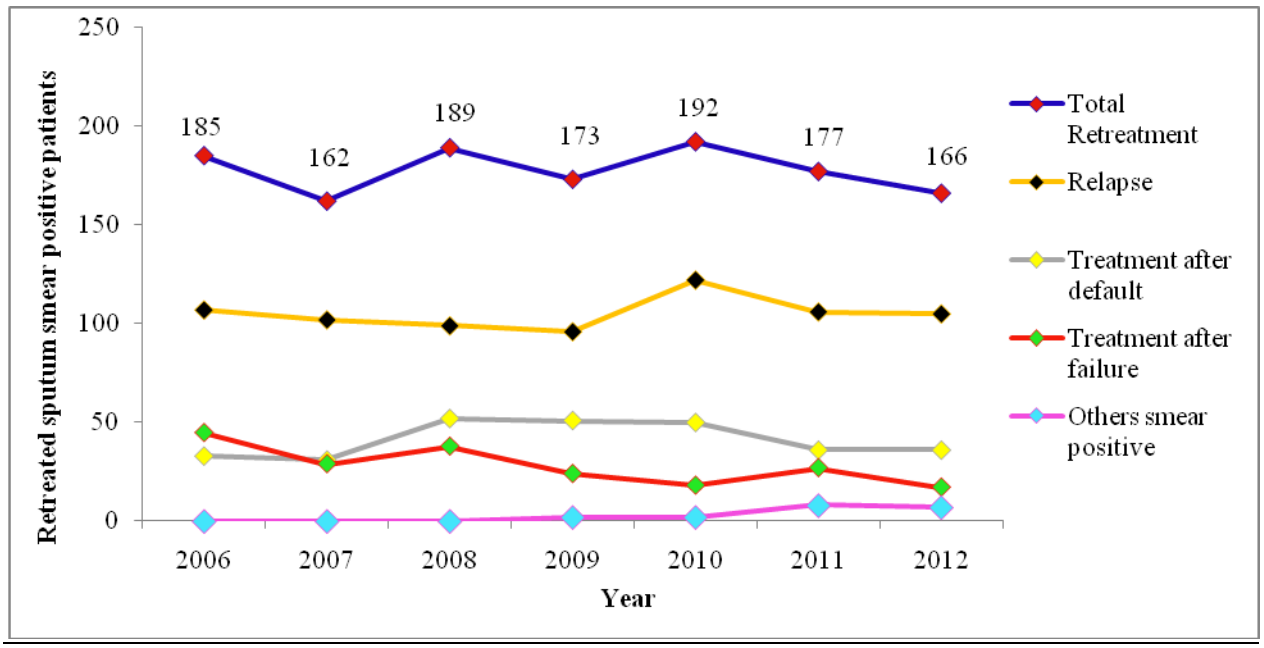


Figure 1: Adamawa state, 2006–2012 TB Retreatment Case Notification[21]

1.3. Justification of the study

The study was predicated on the rising number of TB retreatment patients and the challenges posed by them such as drug wastage, extra cost of retreatment and continuous spread of infection, potentially MDR-TB in the community. In Nigeria, estimated cost of TB treatment per patient year is $79 for initial treatment, $93 for retreatment, $2,368 for MDR-TB and as high as $353 for TB/HIV patients on ART.[22] The study, conducted to identify evidence-based epidemiological information on determinants of retreatment in smear positive patients placed on first line anti-TB drugs in Adamawa state would guide policy formulation, planning interventions, and resource utilization in the enhancement of effective TB treatment in the state. Identified determinants will thus provide the basis for public health action, which will go a long way in controlling and preventing TB retreatment and associated consequences.

1.4. Research questions

1) What are the sociodemographic characteristics, knowledge and attitude of smear positive patients in Adamawa state, from October 2012 to June 2013?
2) What is the knowledge and attitude of smear positive patients associated with retreatment with first line anti-TB drugs (FLADs) in Adamawa state within period of study?
3) What are the sociodemographic factors of smear positive patients associated with retreatment with FLADs in Adamawa state within period of study?
4) What are the adherence (drug and follow-up) factors that could be responsible for being retreated with FLADs in smear positive patients in Adamawa state within period of study?
5) Could TB extent and comorbidity be responsible for being retreated with FLADs in smear positive patients in Adamawa state within period of study?

1.5. General and specific objectives

1.5.1. General Objective:

The overall objective of this study is to identify the determinants of being retreated with first line anti-TB drugs in smear positive patients, and to assess the knowledge and attitude of the patients about TB treatment and prevention in Adamawa state from 4th quarter of 2012 to 2nd quarter of 2013 (October 2012 – June 2013).

1.5.2. Specific objectives:

1. To determine the sociodemographic characteristics, knowledge and attitude of smear positive patients in Adamawa state, from October 2012 to June 2013.
2. To determine the knowledge and attitude of smear positive patients associated with retreatment with first line anti-TB drugs (FLADs) in Adamawa state within period of study.
3. To determine the sociodemographic factors of smear positive patients associated with retreatment with FLADs in Adamawa state within period of study.
4. To determine the adherence (drug and follow-up) factors associated with retreatment with FLADs in smear positive patients in Adamawa state within period of study.
5. To determine the TB extent and comorbidity associated with retreatment with FLADs in smear positive patients in Adamawa state within period of study.

1.6. Hypothesis

1.6.1. The two-tailed null hypotheses, H_O:

There is no association between retreatment with FLADs and exposure risk factors in smear positive patients. $\text{Odds of Exposure}_{\text{Cases}} = \text{Odds of Exposure}_{\text{Controls}}$

1.6.2. Alternate hypothesis, H_A:

There is association between retreatment with FLADs and exposure risk factors in smear positive patients. $Odds\ of\ Exposure_{Cases} \neq Odds\ of\ Exposure_{Controls}$

1.7. Scope of the study

The study was limited to common determinants of retreatment with FLADs in smear positive patients in Adamawa State. Determinants in extra-pulmonary TB and MDR-TB were outside the scope of study. In the state, drug susceptibility testing is not a routine practice and community prevalence survey on MDR-TB is yet to be conducted. On this premise, patients are 'assumed' to have drug-sensitive TB and are generally placed on first line anti-TB regimen with the exception of few cases with clear evidence of MDR-TB who are referred to the National TB and Leprosy Research Centre, Zaria.

CHAPTER TWO: LITERATURE REVIEW

In this document, retreatment included TB patients who failed or defaulted from initial treatment or relapsed after initial treatment success. Literatures were searched from Google scholar, Pubmed, PlosOne, Open access, Biomed Central, Medline and Hinari. Search words were tuberculosis, smear positive, retreatment, first line anti-tuberculosis drugs, determinants, and factors. Search words were combined using Boolean logic. Hard copies of relevant publications also consulted. Review of the literatures within and outside Nigeria document the determinants of retreatment with first line anti-TB drugs to cut across sociodemographic factors and knowledge and attitude about TB treatment and prevention. Others are poor adherence to anti-TB drugs and follow-up visits, severe drug side effects, disease severity and comorbidity.

2.1. Sociodemographic factors

2.1.1. Age and Gender

Studies conducted by Garrido et al 2012 in Brazil and Muture et al 2011 in Kenya, showed that males had 1 – 2 fold risk of being retreated after initial treatment default.[17,18] Garrido et al also found the elderly patients to be protective against retreatment by not defaulting treatment. In 2011 Akpabio and Villiers in South Africa[23] reported TB retreatment to be commoner among the males and in age group 23 – 44 years. In their study, females had reduced risk for retreatment because they adhered better to anti-TB drugs. Similarly, Dooley et al 2011 in Morocco found males to be independently associated with retreatment with higher odds of 2.29 folds compared to controls.[14]

In Sagamu, Nigeria, Daniel et al 2006 found males to have two-fold risk higher of being retreated after initial treatment default.[24] Separate studies conducted in 2011 by Amoran et al in

Ogun and Luka et al in Plateau did not find gender differences to be associated with treatment default.[25,26] Luka et al however shows treatment default to be higher in TB patients age >35 years and those in age groups 16 – 30 and 31 – 45 years.

2.1.2. Employment status and poverty

Studies across the world have shown that TB and treatment outcome are associated with poverty, low income and employment status. In Nepal, Mishra, et al 2005 reported unemployment and low income to be independent risk factor for poor treatment adherence, a precondition for retreatment.[27] Unemployment has also been associated with default and treatment failure in studies reported by Yen et al 2012 in Taipei, Taiwan.[13] In Russia, Jakubowiak et al 2007 also found unemployment as independent risk factor for TB treatment default.[28]

However, in Pakistan, Soomro and Qazi 2009 found employment to be risk factor for TB relapse[29] and in India, Bhagat and Gattani in 2010 also found association between being employed and defaulting retreatment.[30] In Kenya, Muture et al 2011 found that TB patients who earned <10,000 Kenyan Shillings ($114) per month were 5 folds risky of retreatment through and treatment default.[18] In Ibadan, Nigeria, Fatiregun et al 2009 found that high proportion of TB patients with unfavourable treatment outcome were the employed and most of them low income earners of <₦15,000 per month.[31] In Ekiti, Christopher and Bosede 2010 reported that most TB patients were poor with daily spending of <$2 per day.[32] In Ilorin, Nigeria, Salami and Oluboyo 2003 reported unemployment and being unmarried to be associated with poor treatment compliance.[33] In Plateau, Luka et all did not find association between treatment interruption and unemployment.[26]

2.1.3. Clinic proximity

Several studies reported that DOTS clinics sited at a distance of ≥5 km from residence put patients at increased risk of retreatment through initial default or treatment failure. Supportive studies to this are those conducted by Shargie and Lindtjørn 2007 in Southern Ethiopia[34], Namukwaya et al 2011 in Uganda[35] and Boateng et al 2010 in Ghana.[36] However, Erhabor et al 2003 in Ife did not find association between distance and TB treatment compliance.[37] Similarly, Amoran et al 2011 in Ogun did not find association between distance and TB retreatment after initial default.[25] but in a another study in Ogun, Amoran showed that DOTS centres located in a distance >10 km away from residence have about 7 times risk of retreatment through treatment failure.[38] In Plateau, Luka et al in 2011 also documented increased risk of retreatment through initial default among patients residing at a distance ≥5 km from clinic.[26]

2.1.4. Stigma and discrimination

Stigma and discrimination against people with TB is common in communities and is a potent barrier to controlling TB. It isolates people, delays seeking medical help and causes poor adherence to treatment and eventual retreatment. In Thailand, Jittimanee et al 2009 found high level (65%) of stigma among TB patients.[39] In China, Xu et al 2009 reported stigma to increase risk of non-adherence to anti-TB treatment.[40] In Bangladesh, Tasnim et al 2012 found that discrimination against TB patients arises due to misconceptions about TB transmission.[41]

In Ethiopia, Gebremariam et al 2010 shows that stigma with lack of disclosure causes poor treatment adherence.[42] In South Africa, Finlay et al 2012 found stigma to increase by 2 fold the risk of defaulting treatment.[19] Self-stigma among TB patients has been reported in Lagos by Abioye and it was observed to be significantly determined by age, low socio-economic status,

level of education below secondary level, disclosure of status, history of weight loss, previous smoking and alcohol history.[43] Studies conducted by Christopher and Bosede 2010 in Ekiti State of Nigeria shows stigma and discrimination against TB patients to be barriers to health seeking behaviour among TB patients.[32]

2.1.5. Exposure to indoor air pollution, tobacco and alcohol

WHO reported that >70% of households in high TB burden countries, Nigeria inclusive, are exposed to indoor air pollution[4], which has about 2 folds increased risk of TB.[44] Psychoactive substance use is associated with TB retreatment through defaulting treatment, failure or relapse. Smokers have 2 – 3 fold risk for developing or retreating PTB compared to those who never smoked. Lonnroth et al 2011 found that that people who drink alcohol >40g/day have a 3 times increased risk of TB.[45] WHO in 2008 reports that harmful alcohol drinkers with TB disease have 2 – 8 relative risk of TB treatment failure.[4]

In Brazil, Marlucia da Silva Garrido et al 2012 documented that TB patients with alcohol drinking problem have 1.5 times increased risk of TB retreatment through treatment default and they also found alcoholism to independently increase risk of treatment default by 1.5 folds.[17] Batista et al 2008 in Brazil reported smoking to independently increase risk of TB retreatment through relapse by 2 folds.[46] In Taiwan, Chiang et al 2012 showed that tobacco consumption (>20 cigarettes per day) decreased by 77% the odds of cure or treatment completion[47] and in South Korea, Jee et al reported tobacco smoking to increase risk for relapse.[48] Contrary, Jakubowiak et al 2007 in Russia did not find association between tobacco smoking and treatment default.[28] Likewise in Mumbai India, Parikh et al 2012 did not find tobacco and alcohol to be associated with delay in sputum conversion.[15]

In Africa, a cohort study in Uganda showed that daily alcohol consumption have four fold risk of treatment default.[49] Dooley et al 2011 in Morocco reported substance use to have odds of almost 3 times in retreated group compared to controls.[14] Studies in South Africa by Mphothulo et al 2012 found that tobacco use increase risk for TB retreatment[50] and that by Visser et al 2012 show that tobacco smoking delays sputum conversion.[51] In Ilorin, Salami and Oluboyo 2003 found smoking and alcohol consumption to be associated with poor treatment outcome.[33] In Plateau, Nigeria, Luka et all 2011 also reported a 2 fold risk of defaulting treatment among TB patients who smoked tobacco.[26]

2.1.6. Social support and health worker relationship with patients

In China, Xu et al 2009 reported lack of social support to increased the risk of non adherence to anti-TB treatment.[40] They also showed that heavy financial burdens, lack of social support, adverse drug reactions and personal factors were associated with non-adherence. In South Africa, Finlay, et al 2012 found that poor health care worker attitude towards TB patients increases risk of treatment default by 2 folds.[19] In Ghana Boateng et al 2010 showed that family support independently protects against defaulting treatment by 0.29 times.[36]

2.2. Knowledge and attitude of patients

In India, Vijay et al 2010 reported that poor TB knowledge increases risk of being retreated after treatment default[52] and in Brazil, Garrido et al 2012 found that TB patients with low education level have higher risk of being retreated.[17] Studies by Cramm et al 2010 in South Africa[53] and Ngadaya et al 2009 in Tanzania[54] reported that poor TB knowledge increases risk of being retreated after treatment default. In Uganda, Obuku et al 2012 reported low knowledge among

TB patients in the areas of TB cause, clinical features, transmission, prevention, free treatment but higher knowledge in aspects of curability and treatment.[55] In Kenya, Muture et al 2011 found that TB patients with inadequate knowledge of TB had 8 times increased risk of treatment default.[18]

In Ibadan, Fatiregun et al 2009 shows that PTB patients with poor knowledge of TB have higher risk of poor treatment outcome such as default, relapse, failure or death.[31] However in Ekiti, Christopher and Bosede in 2010 found TB patients to have satisfactory knowledge about the disease except in the areas of stigma and discrimination.[32] In Plateau, Luka et al 2011 found that lack of knowledge about duration of TB treatment increases patients risk for treatment default.[26]

2.3. Drugs supply, adherence, concomitant ingestion of herbal preparations

Universal access to high-quality drugs is central to the Global Plan to Stop TB. The Global Drug Facility (GDF) is the frontline concerned with supply of affordable, quality-assured drugs to countries in need.[56] Uninterrupted drug supply and choice of fixed-dose combination will therefore increase patience adherence. Drugs out of stock and missing of anti-TB doses especially in the intensive phase increases risk of retreatment.

In India, Vijay et al 2010 found that patient who missed anti-TB doses had increased risk of being retreated through initial treatment default.[52] Same have been reported in China, by Ai et al 2010 and Morocco, by Dooley et al 2011.[14,57] In Uganda, Namukwaya et al 2011 showed that patients who missed ≥14 doses of anti-TB and ≥14 days of clinic appointment dates had increased risk of treatment failure. Namukwaya et al, further found that patients who missed appointment dates for ≥14 days were independent risk factor for the treatment failure.[35] In

Uganda, Anyama et al 2007 on the contrary did not find association between retreatment and patients that ever missed anti-TB doses.[58]

Concomitant ingestion of herbal preparations reduces potency and amplifies side effects of anti-TB drugs. In Kenya, Muture et al 2011 found that concurrent use of herbal medication among TB patients had almost 6 folds odds higher among defaulters compared to controls.[18] In Zambia, Kaona et al 2004 reported that shortage of drugs at home increase chances of non-compliance to treatment in TB patients.[59] Drug unavailability has also been shown by Kandel et al 2008 in South Africa[60] and by Ayisi et al 2011 in Kenya[61] as one of the reasons why patients interrupt or default their treatment. In Ekiti, Christopher and Bosede 2010 identified use of unorthodox care to be common among the females TB patients.[32]

In Ilorin Bello and Itiola 2010 in their study identified very high drug adherence among TB patients.[62] In University of Maiduguri Teaching Hospital, Nigeria, Yakubu et al 2012 reported that supply of anti-TB drugs to patients was continuous and that resulted in high treatment success rate.[63]

2.4. TB extent and comorbidity

2.4.1. TB/HIV comorbidity

TB/HIV interacts with each other at the level of disease progression and drug treatment. HIV is the most potent risk factor for TB and people living with HIV who are also infected with TB are 21 – 34 times more likely to develop active TB compared to TB patients who are HIV-negative.[10] HIV infection increases risk for recurrent TB, which may be due to either TB relapse or re-infection.[64,65] Concomitant treatment of TB/HIV can be complicated by factors such as

overlapping drug toxicities, drug-drug interactions, and poor adherence to drugs thereby increasing the risk for retreatment.

In Brazil, Garrido et al 2012 shows that TB/HIV co-infection increases risk of default by 1.6 times.[17] Similar risk had been reported by Muture et al 2011 in Kenya[18], Arentz et al 2011 in Mombasa, Kenya[66] and Burton et al 2011 in Ghana.[67] On the contrary, Nyamogoba et al 2012 in Kenya did not find association between TB/HIV co-infection and retreatment from relapse or re-infection.[68] Study in South Africa by Mphothulo et al 2012 did not find association between TB/HIV and re-infection or failure.[50] and in Uganda Anyama et al 2007 also did not find association between TB/HIV and retreatment.[58]

Increased risk of retreatment in TB/HIV co-infection had also been reported by Ifebunandu et al 2012 in Abakaliki, Nigeria[69] and by Ige and Oladokun in University College Hospital Ibadan through treatment failure.[70] However, Daniel et al 2006 in Sagamu[24] and Amoran[25] in Ogun did not find association between TB/HIV co-infection and retreatment secondary to treatment default. In Gombe, Northeastern Nigeria, Jibrin et al likewise did not find association between TB/HIV co-infection and retreatment secondary to treatment failure.[71]

2.4.2. TB/Diabetes comorbidity:

TB/ diabetes mellitus (DM) interacts with each other at the level of the disease and through dug-drug interaction. DM suppresses immunity leading to multisystemic infection, triples the risk of developing TB and makes glycaemia control worse in TB/DM co-morbidity.[45] TB/DM comorbidity has a higher risk of TB retreatment through relapse, failure or default. Systematic

review by Baker et al 2011 show DM to be associated with TB treatment failure and death combined together by an almost 2-fold risk.[16].

According to studies by Ruslami et al 2010 and Amrit Guptan 2000 DM may be associated with decreased rifampicin concentrations, which may result from drug–drug interactions between anti-TB drugs and oral hypoglycaemic drugs. Anti-TB drug, rifampicin, a potent hepatic enzyme-inducer, hampers glycaemic control by increasing the metabolism of most oral anti-hyperglycaemic agents, especially sulphonylureas and biguanides, and thus reduces their plasma levels, leading to hyperglycaemia and resultant treatment failure or relapse after treatment.[72,73] In pre-diabetes, rifampicin, accelerates the intestinal absorption of glucose and may exaggerate the symptoms of diabetes.[74]

In Southern Mexico, Jiménez-corona et al 2012 reported a risk of 2.93 for TB treatment failure in TB/DM co-infection.[75] In contrast, study in Pakistan by Soomro and Qazi 2009 did not find association between TB/DM and relapse.[29] and in Uganda Anyama et al 2007 did not also find association between TB/DM and retreatment.[58]

2.4.3. AFB smear density, extensive lung cavitations and body mass index

High pretreatment smear density is reported to delay sputum conversion. This may linger leading to treatment failure. Khan et al 2006 found that low body mass index (BMI) at diagnosis and poor weight gain of ≤5% was associated with increases risk of relapse by 2-folds.[76] Study by Khurram et al 2009 in Pakistan found that males had more weight loss at diagnosis and less weight gain at the end of treatment.[77] A study in Pakistan by Soomro and Qazi 2009 did not find association between relapse and being underweight at diagnosis but with inability to gain weight

while on treatment.[29] In Mumbai India, Parikh et al 2012 showed that high pretreatment smear density and extensive lung cavitations were associated with delay sputum conversion leading to increased risk for retreatment.[15]

In Uganda, Namukwaya et al 2011 showed that risk of retreatment secondary to treatment failure was increased in those with high pretreatment smear density (AFB 3^{+}) and in those with extensive lung cavitations even though they were not independent predictors.[35] In Morocco, Dooley et al 2011 further showed that patients who remained smear positive after 3 months of treatment had 7 times higher risk of being retreated.[14]

2.4.4. Adverse drug effect:

In China, Xu et al 2009 in an in-depth interview found adverse drug reactions, and social stigma to be additional potential factors for non-adherence.[40] In the same China, Ai et al 2010 found that TB patients with adverse effects of drugs had tendency to interrupt their treatment.[57] In Ghana Boaeteng et al 2010 shows that adverse drug side effect increases risk of defaulting treatment by 3-folds.[36] In contrast, study in Uganda by Namukwaya et al in 2011 did not find association between adverse effects of drugs and treatment failure.[35]

CHAPTER THREE: METHODOLOGY

3.1. Description of study area

Adamawa state is located in North Eastern part of Nigeria and lies between latitude 8^0N and 11^0N, and longitude 11.5^0E and 13.5^0E.[78] The state is bounded by Borno State to the North, Gombe and Taraba States to the North/West and South/West respectively, and the Cameroons extending throughout its Eastern border. Adamawa state has three Senatorial zones (central, north and south), 21 local government areas (LGAs), 37 Development Areas, 226 Political Wards and 120 DOTS clinics. Yola is the state capital and sit of the government. Adamawa state has a population density of 95 person/km^2 arising from a population of over 3.7 million (projected from 2006 National Population Census) with a land mass of 39,742.12 km^2.[78]

The State is multi-ethnic in composition; Hausa and Fulani are widely spoken. Other languages include Higgi, Marghi, Kilba, Bura, Bachama, Lunguda and Chamba. Farming, fishing, livestock rearing and business/trading are the main occupation. As at 2010, Adamawa State had over 1,290 health facilities which included; 1 Federal Medical Centre and 6 General, 1 Dermatological, and 7 Cottage Hospitals. The remaining were Clinics, Dispensaries, and Health Posts. Over 1,160 facilities were public while 137 private (12%); 109 of these provided leprosy control services while 120 provided TB Control Services. The study was conducted in 12 LGAs: Mubi North, Michika, Madagali, Mubi South, Yola South, Gombi, Fufore, Hong LGA, Mayo-Belwa, Lamurde, Jada and Numan.

3.2. Study design

Unmatched case-control study involving smear positive patients enrolled into TB treatment programme from the 4th quarter of 2012 to 2nd Quarter of 2013 i.e. October 2012 – June 2013.

Cases were PTB patients, age ≥15 years, on retreatment regimen with first line anti-TB drugs (FLAD), and with a pretreatment smear positive result. Controls were PTB patients, age ≥15 years, with pretreatment smear positive result and converted to smear negative result in 5th month (or later) while on the initial treatment with FLAD, and in whom there is no default, failure or relapse.

3.3. Study population

3.3.1. Inclusion criteria

1) Study subjects that resided in Adamawa state for at least 6 months before commencement of treatment with FLADs.
2) Cases that were at least 15 years of age and currently on retreatment regimen with FLADs after initial default, failure or relapse.
3) Controls that were at least 15 years of age and currently on initial treatment regimen with FLADs, converted to smear negative in 5th month (or later) and in whom there is no default, failure or relapse.

3.3.2. Exclusion criteria

1) All patients that were less than 15 years of age within the period of study.
2) All patients diagnosed with extra-pulmonary TB.

3) All patients placed on anti-TB other than FLADs.

4) All patients on WHO DOTS transferred in from DOTS clinics outside Adamawa state.

5) Controls who had documented history of default or with smear positive result in the 5th month of their treatment.

3.4. Sample size determination

A minimum sample size of 243 (cases = 81; controls 162) calculated using Fleiss formula with continuity correction, generated from OpenEpi version 2.3.

$$n_1 = \frac{\left[Z_{1-\alpha/2}\sqrt{(r+1)\,\bar{p}\,\bar{q}} + Z_{1-\beta}\sqrt{rp_1q_1 + p_2q_2}\right]^2}{r(p_1 - p_2)^2} + \frac{1}{1-f}$$

n_1 = sample size for cases (generated by OpenEpi)

$n_2 = 2 \times n_1$ = sample size for controls (generated by OpenEpi)

P_2= proportion of controls with non-adherence = 15% (Adamawa SMOH 2010)

P_1 = proportion of cases with exposure = 34.62% (generated by OpenEpi)

r = ratio of cases to controls = 1:2

OR = least extreme odds ratio to be detected = 3.0

$Z_{1-\beta}$ = Z-score for one-tailed test on β level = 1.282 (where β = 1 – power to detect = 1 – 90%)

$Z_{1-\alpha/2}$ = Z-score for two-tailed test on α level = 1.96 (where α level set at 5% with a corresponding confidence level, 95%)

$\bar{p} = \frac{p_1 + rp_2}{r+1}$ $\quad \bar{q} = 1 - \bar{p}$ f = non-response rate = 10%

Table 4: Sample size by Fleiss formula with continuity correction

	Sample Size for Unmatched Case-Control Study		
	Kelsey	**Fleiss**	**Fleiss with continuity correction**
Sample size: cases	70	74	81
Sample size: controls	139	147	162
Total sample size	209	221	243

3.5. Sampling technique

Adamawa state has 3 senatorial districts, 21 Local Governments Areas (LGAs) and 120 DOTS centres. A multistage sampling technique was adopted.

Stage 1: DOTS central register of the 21 LGAs were reviewed and LGAs with high retreatment caseload ranked according to Senatorial district. The first four LGAs with high retreatment caseload in each Senatorial district were selected.

Table 5: Sample size allocation

North Senatorial District			**Central Senatorial District**			**South Senatorial District**		
LGA	**Case**	**Control**	**LGA**	**Case**	**Control**	**LGA**	**Case**	**Control**
Mubi North	6	12	Yola South	12	24	Mayo-Belwa	14	28
Mubi South	7	14	Gombi	6	12	Lamurde	7	14
Michika	3	6	Fufore	5	10	Jada	6	12
Madagali	3	6	Hong	6	12	Numan	6	12
Total	**19**	**38**	**Total**	**29**	**58**	**Total**	**33**	**66**

Stage 2: Using simple random sampling technique, four DOTS centres with high retreatment caseload were selected from the selected LGAs in stage 1. Calculated sample size allocated proportionately to the selected DOTS centres.

Stage 3: Using systematic random sampling technique, study subjects that met the inclusion criteria in stage 2 were recruited. Patients on retreatment regimen and with smear positive results at diagnosis were included as cases. Patients with smear positive results at diagnosis and negative at 5^{th} month (or later) while on initial treatment but without default, failure, or early relapse were included as controls. Cases and controls underwent same face-to-face interview,

examinations and screening using the same instrument (structured questionnaire and screening equipment). Subjects who declined study where replaced with the next immediate ones in the same systematic order. Each subject was assigned unique identifying code number for tracking during analyses.

3.6. Study instruments and materials

Study instruments and materials used included TB DOTS registers at the LGA and health facility level to determine caseload. Questionnaire used was modified from the studies conducted in Uganda by Namukaya et al and Anyama et al.[35,58] Questionnaire was structured with both open and closed ended questions to obtain information from study subjects. HIV screening kits (Determine, Unigold and STATpak) deployed to screen subjects for HIV especially in subjects not screened prior to study period. Standardized blood glucose screening machine and test strips (Acucheck®) used to screen subjects for diabetes. Weighing scale and heightometer used to measure weights and height.

3.7. Data collection methods

Data were collected through face-to-face interview using semi structured pre-tested questionnaires by trained community health workers who communicate well in Hausa and Fulfude languages. Questionnaire contained sections on demography; socio-economy; past medical history; physical examination and laboratory diagnosis/screening; and knowledge and attitude. At the physical examination and laboratory stage, anthropometric measurements were conducted with body weight in kilograms and height in metres. Blood was screened for diabetes and HIV after counseling for patients that were not screened for HIV in the course of TB treatment. Available chest radiographs that were not reported were also reviewed.

3.8. Measurement of variables

We recorded information on sociodemographic characteristics; HIV, DM and other comorbidity status; tobacco and alcohol use status; nature and method of cooking. Others included drug side effects encountered; lung cavitations in chest X-rays. Cigarette quantity measured and expressed in pack-years. Blood glucose level measured using the WHO protocol. We also recorded sputum smear density in the register. Weight and height were measured to the nearest 0.1 kg and 0.1 cm respectively with the subject bare feet and with minimal clothing. Alcoholism was assessed using the CAGE proxy tool designed in 1984 by Ewing JA.[79]

Table 6: CAGE proxy characteristic for assessment of alcoholism[79]

CAGE characteristic	Yes	No
Have you felt the need to *Cut down* on your drinking?		
Do you feel *Annoyed* by people complaining about your drinking?		
Do you ever feel *Guilty* about your drinking?		
Do you ever drink an *Eye-opener* in the morning to relieve shakes?		

Two or more affirmative responses suggest problem drinking (alcoholism).

Knowledge and attitude were assessed using 8 and 3 component questions respectively. Maximum of one (1) and minimum of zero (0) mark was awarded to each component taking into account the number of plausible responses provided by subjects. Scores for knowledge and attitude were separately summed up and mean scores calculated. Minimum score of 50% was considered as the minimum pass mark for the studied population.

Knowledge: 1 score per question (maximum percent score = 8/8 x 100 = 100%)

1. What is the cause of tuberculosis (TB) of the lungs?
2. How can someone be infected with the agent that causes TB of the lungs?
3. What are the conditions, situations/illnesses that can put someone at risk of developing TB?
4. Mention the common symptoms/signs that can make you suspect someone of having TB.
5. How can TB be prevented?
6. Is TB curable/treatable? If yes, how can it be cured/treated?
7. For how long can a patient be on anti-TB drugs, initial treatment and retreatment?
8. Are there consequences of not completing TB treatment? If yes, mention the consequences of not completing TB treatment.

Attitude: 1 score per question (maximum percent score = 3/3 x 100 = 100%)

1. What advices will you give to someone you suspect has TB?
2. What advices will you give to someone placed on anti-TB drugs?
3. What are the things you do to improve your health since you started anti-TB drugs?

3.8.1. Statistical Analyses

Data crosschecked, cleaned and double entered into Microsoft Office Excel 2007. Univariate, bivariate and unconditional multiple logistic regression analysis conducted using Epi Info version 3.4.3 statistical software set at 5% alpha level of significance and 95% confidence. Two-tailed Yates-corrected chi-square or Fisher exact test (for cells with values less than 5) used to assess categorical variables. We used odds ratios as measure of association at corresponding 95% confidence intervals calculated using Taylor series. We described frequency distribution of selected sociodemographic characteristics in univariate stage and odds ratio measure of

association obtained in bivariate analysis. Both borderline and statistically significant variables at the two-tailed level in bivariate analysis were entered into unconditional multiple logistic regression model. While controlling for 'potential confounders' and 'effect modifiers' backward elimination approach applied until a regressed model that best identified independent and combined risk factor predictors were determined.

3.9. Ethical issues

Ethical clearance, processed from the Health Research Ethics Committee in Adamawa State (Ref.No S/MOH/1131/I/24). Informed written/oral consent obtained from the subjects after they have understood the purpose, methods, anticipated benefits and potential risks involved in the study. Ethical principles prescribed by Belmont observed strictly.[80] Subjects were respected for their rights to privacy and confidentiality; cultural differences; and voluntary withdrawal from the study. While ensuring that risk did not outweigh benefit, all subjects regardless of gender or socioeconomic status were treated fairly.

3.10. Limitation

Inability to screen subjects for drug resistant TB. In Adamawa state, drug susceptibility testing is not a routine practice due to resource constraint. The retreated cases due to relapse cases could have been mixed with re-infection because the dividing line between re-infection and true TB relapse is ambiguous and controversial. Severity of disease based on lung cavitations could not be ascertained due to unavailability of chest radiographs. Haematological parameters such as packed cell volume, white cell count and CD4 cell count were not done. These could have provided additional information on disease severity. Like any other case-control study, recall biases could not have been completely avoided.

CHAPTER FOUR: RESULTS

4.1. Sociodemographic characteristics

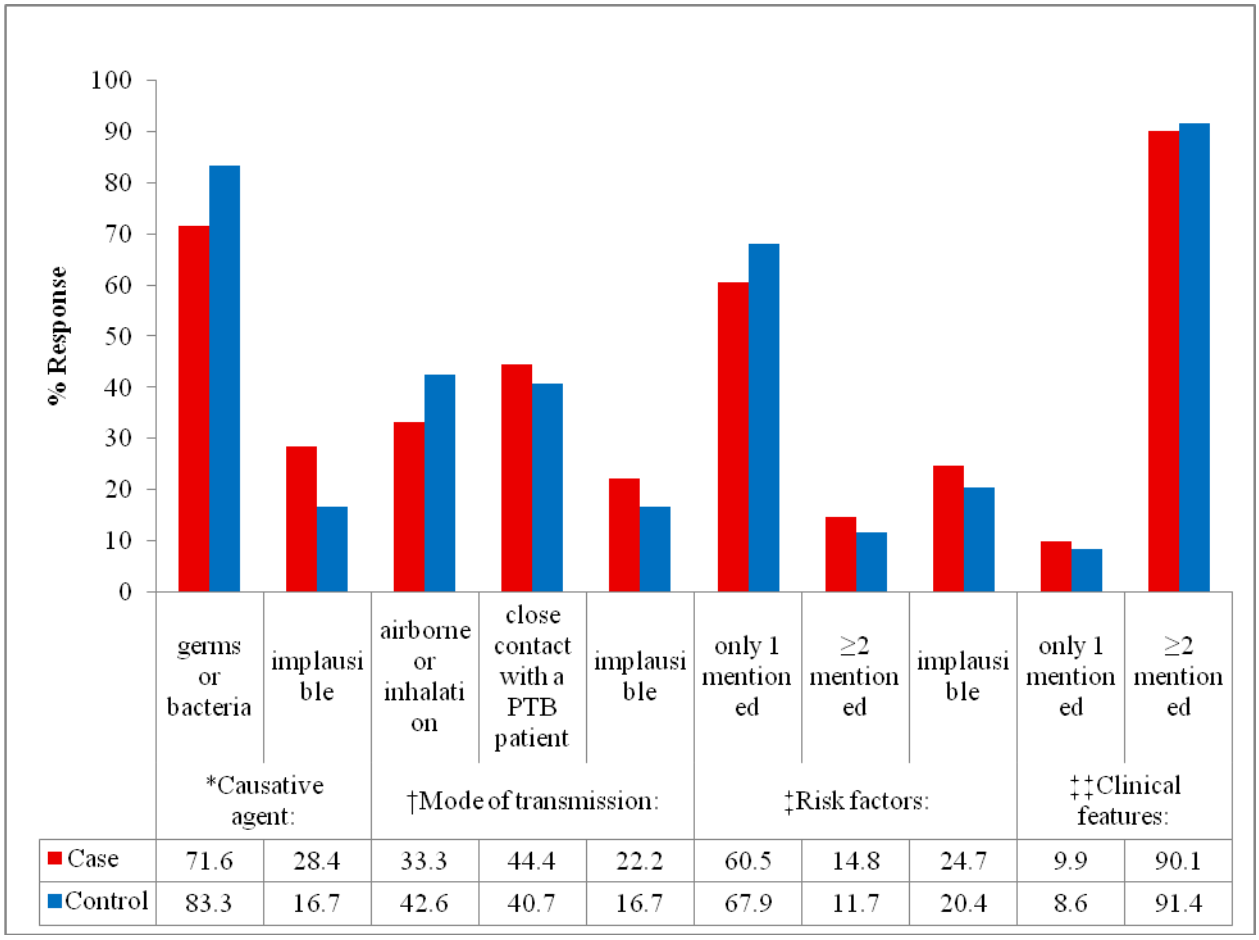
Table 7: Sociodemographic distribution among cases and controls

Characteristic	Cases (n = 81)	Controls (n = 162)
	Percent (%)	Percent (%)
Age classification:		
Adolescents (14 – 19 yrs)	0.0	9.9
Young adults (20 – 40 yrs)	71.6	69.8
Middle-aged adults (41 – 59 yrs)	23.5	13.5
Elderly (60+ yrs)	4.9	6.8
Mean age (35.2 ± 11.7 yrs)	37.8 ± 10.6	33.9 ± 12.0
Gender:		
Male	79.0	64.2
Female	21.0	35.8
Tribe:		
Fulani	22.2	31.5
Bwatiye	11.1	8.0
Kilba (Huba)	9.9	8.0
Hausa	7.4	6.2
Chamba	7.4	2.5
Margi	6.2	4.3
Others	35.8	39.5
Religion:		
Islam	53.1	56.2
Christianity	46.9	43.8
Marital status:		
Single	39.5	33.3
Married	56.8	60.5
Widowed	2.5	2.5
Divorced	1.2	3.7
Highest educational level attained:		
No formal	12.3	15.4
Koranic	6.2	9.9
Primary	23.5	11.1
Secondary	44.4	46.9
Tertiary	13.6	16.7
Occupation:		
Government employees	18.5	19.1
Business	35.8	46.9
Large scale farming	1.3	4.3
Subsistence farming/labourer	18.5	9.9
Not employed	25.9	19.8

Table 7 Summary: Demographic distribution among cases and controls

Of 243 patients studied (81 cases, 162 controls), mean age overall 35.2 ± 11.7 years (cases 37.8 ± 10.6; controls 33.9 ± 12.0). Young adults 20 – 40 years constituted 70.4% (cases 71.6%; controls 69.8%) although there was no retreatment among the adolescents group. Also, very few elderly subjects were recorded (cases 4.9%; controls 6.8%). The males represented 69.1% (cases 79.0%; controls 64.2%).The Fulani ethnic extraction was the highest recruited with cases 22.2% and controls 31.5%. The married represented 56.8% cases and 60.5% controls. Majority of subjects had secondary education of which cases 44.4% and controls 46.9%. Business was the highest reported occupation with 35.8% cases and 46.9% controls. The unemployed constituted 25.9% cases and 19.8% controls.

4.2. Knowledge and attitude responses among cases and controls



	*Causative agent:		†Mode of transmission:			‡Risk factors:			‡‡Clinical features:	
Case	71.6	28.4	33.3	44.4	22.2	60.5	14.8	24.7	9.9	90.1
Control	83.3	16.7	42.6	40.7	16.7	67.9	11.7	20.4	8.6	91.4

Figure 2: Knowledge assessment responses on PTB by subjects

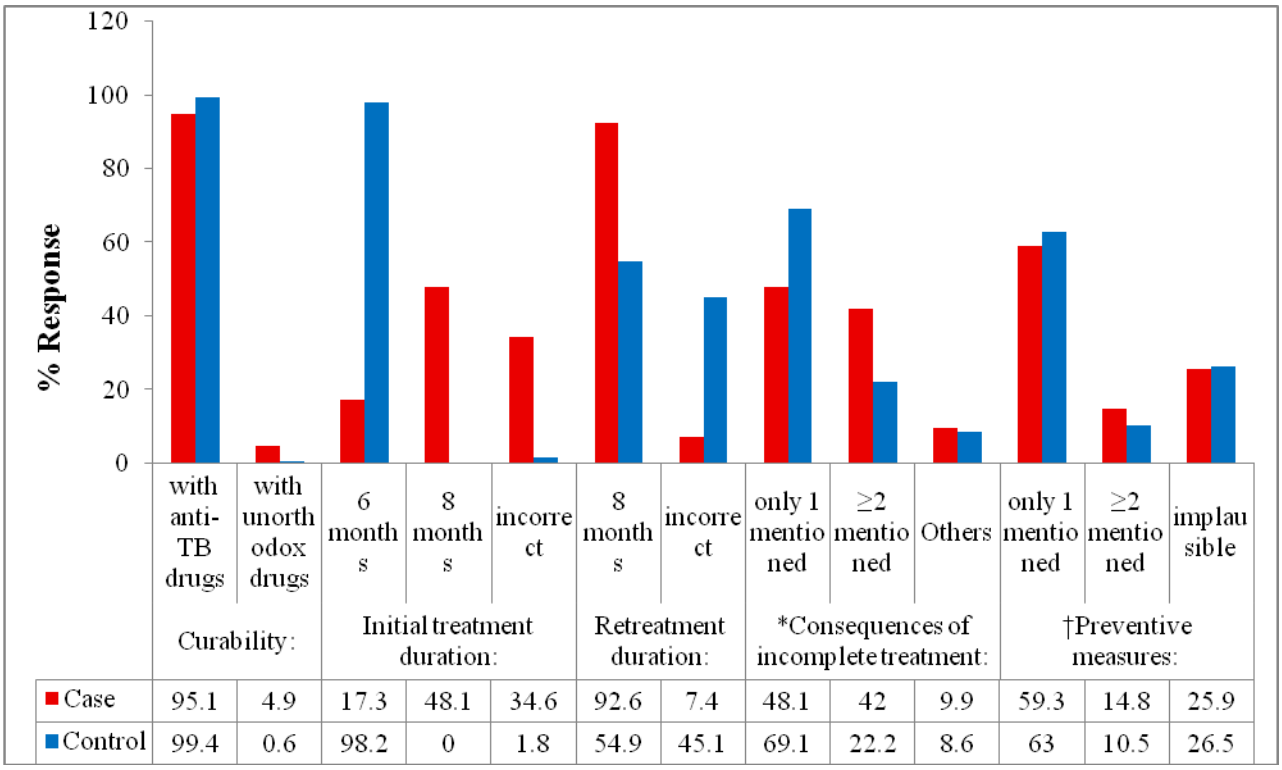
*__Implausible:__ *cold weather, enemy, evil spirit, air, HIV, tobacco smoking, any illness, don't know, and I forgot.*

†__Implausible:__ *Living together, eating/drinking together, sharing objects, dust, don't know, cold weather, and smoke.*

‡__Risk factors: (a) plausible-__ *close contact with a TB patient, smoking, diabetes, HIV infection, low immunity, poverty, poor nutrition, alcohol drinking, poor environmental and personal hygiene.*

(b) implausible- *relating with HIV patient, cough, 'frequent illness', contaminated drinks, peppery foods, chilled drinks, kola nuts, eating with a TB patient, cold weather, sexual promiscuity, pneumonia, will of God, strenuous jobs, stopping medication, and don't know.*

‡‡__Clinical features: plausible-__ *cough, coughing out sputum with/without blood, fever, tiredness, body weakness, weight loss, poor appetite, dizziness, night sweat, and shortage of blood.*

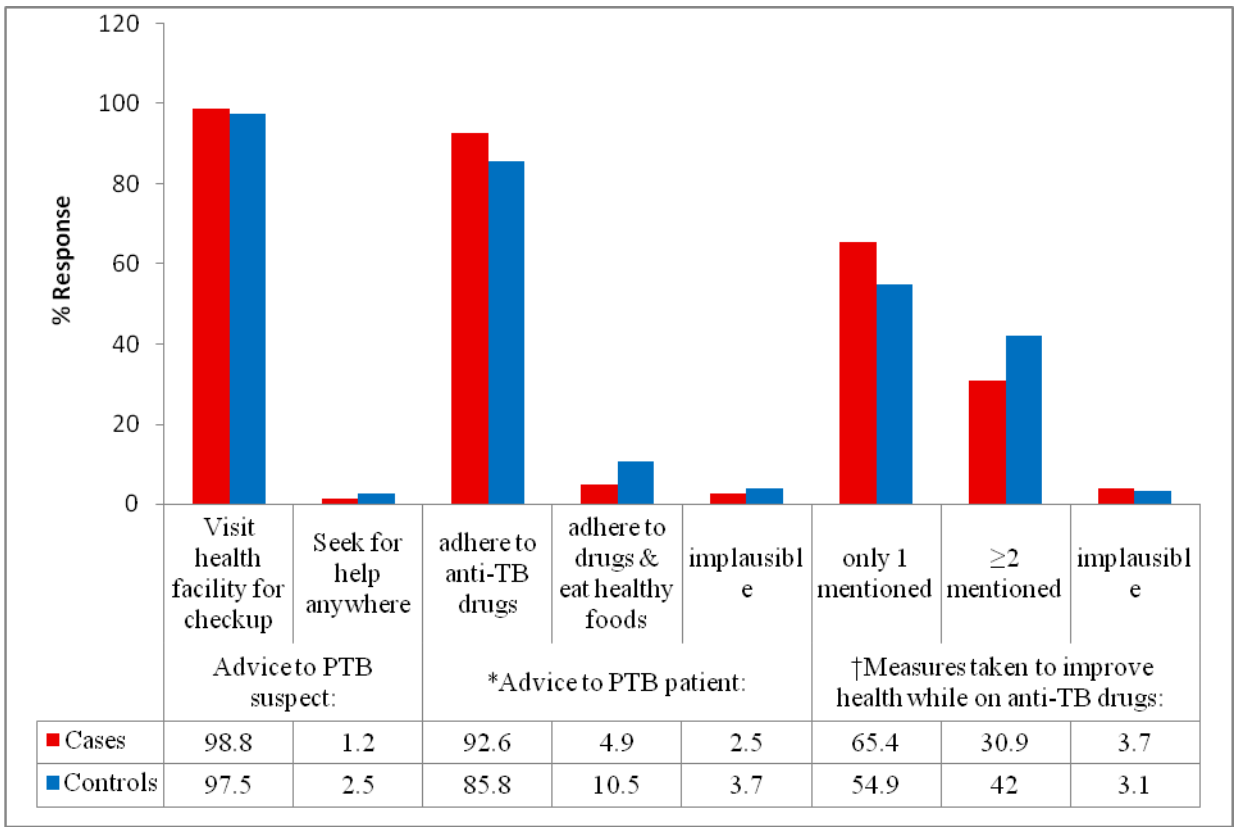


	with anti-TB drugs	with unorthodox drugs	6 months	8 months	incorrect	8 months	incorrect	only 1 mentioned	≥2 mentioned	Others	only 1 mentioned	≥2 mentioned	implausible
	Curability:		Initial treatment duration:			Retreatment duration:		*Consequences of incomplete treatment:			†Preventive measures:		
Case	95.1	4.9	17.3	48.1	34.6	92.6	7.4	48.1	42	9.9	59.3	14.8	25.9
Control	99.4	0.6	98.2	0	1.8	54.9	45.1	69.1	22.2	8.6	63	10.5	26.5

Figure 3: Knowledge assessment responses on PTB by subjects

[*]**Consequences:** *'sickness will be severe, TB can kill, sickness will not be cured, retreatment, fear of drug resistance, sickness will spread to other people.* Others: health workers will quarrel me, people will take me unserious, people will discriminated against me, and anything can happen with me'.

[†]**Preventive measures: (a) plausible-** *regular medical checkup, avoid smoking, cough ethics, screen people with cough, reduce/avoid alcohol, immunization, avoid HIV, treat HIV and diabetes, warm environment, campaign against tobacco industries, eat healthy foods, health education people, cross ventilation, personal hygiene, and environmental sanitation.*
(b) implausible- *avoid cats/foods contaminated by cats, avoid eating or relating with people that have TB, avoid cold environment, prayers, 'take any drug', stay in one place, I don't know, and reduce smoking.*



	Visit health facility for checkup	Seek for help anywhere	adhere to anti-TB drugs	adhere to drugs & eat healthy foods	implausible	only 1 mentioned	≥2 mentioned	implausible
	Advice to PTB suspect:		*Advice to PTB patient:			†Measures taken to improve health while on anti-TB drugs:		
Cases	98.8	1.2	92.6	4.9	2.5	65.4	30.9	3.7
Controls	97.5	2.5	85.8	10.5	3.7	54.9	42	3.1

Figure 4: Attitude assessment responses on PTB by subjects

[*]**Advice to PTB patient: (a) plausible-** adhere *to anti-TB drugs, and eat healthy foods.*
(b) implausible- *'stay in one place, take herbs together with anti-TB, take anti-TB until you feel better, and seek for other help'.*

[†]**Measures taken to improve health: (a) plausible-** *adhere to treatment, adequate rest, avoid smoking, avoid alcohol, avoid strenuous jobs, and eat healthy foods with lots of fruits and vegetables (e.g. Moringer oleifera).*
(b) implausible- *stop going out, avoid chilled drinks, avoid cold weather, I don't have money, and I'll do nothing.*

4.3. Association between retreatment and knowledge and attitude

Table 8: Association between retreatment and knowledge assessment score

Factor	Cases (n = 81)	Controls (n =162)	Crude OR	95% CI: LL, UL	P value
Overall knowledge score					
(mean score = 69.97 ± 11.21%)					
score <69.97%	36	53	1.64	0.95, 2.84	0.099
score ≥69.97%	45	109			
Causative agent					
(mean score = 80.74 ± 38.4%)					
score <80.74%	23	27	1.98	1.05, 3.74	0.049
score ≥80.74%	58	135			
Mode of transmission					
(mean score = 81.89 ± 38.59%)					
score <81.89%	18	26	1.49	0.76, 2.92	0.32
score ≥81.89%	63	136			
Risk factors					
(mean score = 28.64 ± 21.03%)					
score <28.64%	22	35	1.35	0.73, 2.50	0.422
score ≥28.64%	59	127			
Symptoms and signs					
(mean score = 73.46 ± 18.31%)					
score <73.46%	64	123	1.19	0.62, 2.27	0.71
score ≥73.46%	17	127			
Curability†					
(mean score = 98.68 ± 9.53%)					
score <98.68%	4	1	8.36	0.92, 76.1	0.087
score ≥98.68%	77	161			
Treatment duration					
(mean score = 77.78 ± 25.31%)					
score <77.78%	31	76	0.70	0.41, 1.21	0.253
score ≥77.78%	50	86			
Consequence of not completing treatment					
(mean score = 92.22 ± 25.18%)					
score <92.22%	8	15	1.074	0.43, 2.65	0.938
score ≥92.22%	73	147			
Preventive measures					
(mean score = 26.38 ± 20.33%)					
score <26.38%	23	42	1.13	0.62, 2.06	0.798
score ≥26.38%	58	120			

†Fisher exact test used as cell frequency <5

Table 8 Summary: Association between retreatment and knowledge assessment score

The overall mean knowledge score was approximately 70.0% and this would have been higher if not for the low scores recorded for knowledge about risk factors (mean score, 28.64 ± 21.03%) and preventive measures (mean score, 26.38 ± 20.33%). Only 45 (55.6%) cases and 109 (67.3%) controls scored above the overall mean knowledge score.

There was a statistically significant difference in knowledge about causative agent (mean score = 80.74 ± 38.4%) among cases and controls. Score <80.74% about knowledge on causative agent has almost 2-folds odds higher among the retreatment group compared to controls (cOR 1.98; 95% CI: 1.05-3.74)

Table 9: Association between retreatment and attitude assessment score

Factor	Cases (n = 81)	Controls (n =162)	Crude OR	95% CI: LL, UL	P value
Overall mean attitude score (mean score = 47.22 ± 8.47%)					
score <47.22%	53	85	1.71	0.99, 2.98	0.074
score ≥47.22%	28	77			
Advice to PTB suspect† (mean score = 49.26 ± 7.00%)					
score <49.26%	1	6	0.32	0.01, 2.76	0.519
score ≥49.26%	80	156			
Advice to PTB patient (mean score = 49.92 ± 9.96%)					
score <49.92%	5	11	0.90	0.30, 2.69	0.927
score ≥49.92%	76	151			
Measures taken to improve health while on anti-TB drugs (mean score = 42.47 ± 18.91%)					
score <42.47%	54	86	1.77	1.01, 3.08	0.059
score ≥42.47%	27	76			

†Fisher exact test used as cell frequency <5

Table 9 Summary: Association between retreatment and attitude assessment performance

The component and overall mean attitude scores recorded were all below the set benchmark score of 50.0%. Only 28 (34.6%) cases and 77 (47.5%) controls scored above the overall mean attitude score of 47.22 ± 8.47%. Association between cases and controls could not achieve statistical significance. However, score <42.47% about attitudinal measures to improve health while on anti-TB drugs was almost statistically significant with 1.8 odds higher in the retreatment group compared to controls (cOR 1.8; 95% CI: 1.01, 3.08)

4.4. Association between retreatment and sociodemographic factors

Table 10: Association between retreatment and sociodemographic factors

Factor	Cases (n = 81)	Controls (n =162)	Crude OR	95% CI: LL, UL	P value
Age in years:					
≥41(Middle-aged adults/elderly)	23	33	1.55	0.84, 2.87	0.215
15 – 40 (Adolescents/young adults)	58	129			
Gender:					
Male	64	104	2.10	1.13, 3.92	0.027
Female	17	58			
Marital status:					
Single/divorced/widowed	35	64	1.16	0.68, 2.00	0.678
Married	46	98			
Employment status:					
Unemployed	21	32	1.42	0.76, 2.67	0.350
Employed	60	130			
Highest education level attained:					
Below secondary	34	59	1.26	0.73, 2.18	0.484
Above secondary	47	103			
Distance, house to clinic:					
≥5 km	13	11	2.62	1.12, 6.16	0.04
<5 km	68	151			
Daily transport fare to clinic:					
≥₦500	13	23	1.16	0.55, 2.42	0.848
<₦500	68	139			
Ever smoked tobacco†:					
Yes	43	51	2.46	1.42, 4.26	0.0018
No	38	111			
Quantity of tobacco ever smoked daily†:					
≥11cigarettes	20	11	3.16	1.29, 7.75	0.019
<11cigarettes	23	40			
Ever consumed alcohol†:					
Yes	36	40	2.44	1.39, 4.29	0.0028
No	45	122			
Alcoholism assessed by CAGE tool among current drinkers†:					
≥2 points	25	17	3.07	1.19, 7.92	0.033
<2 points	11	23			
Ever discriminated against by people:					
Yes	24	26	2.2	1.17, 4.16	0.021
No	57	136			
Cooking method in household‡:					
Firewood/charcoal	77	152	1.27	0.35, 5.71	0.946
Kerosene stove	4	10			

†Ever consumed alcohol or smoked tobacco till at least treatment onset
‡Fisher exact test used as cell frequency <5

Table 10 Summary: Association between retreatment and sociodemographic determinants

Males have 2-folds odds higher of being retreated than controls (cOR 2.1; 95% CI: 1.13-3.92). Similarly, discrimination (cOR 2.2; 95% CI: 1.17-4.16) and exposure to alcohol (cOR 2.4; 95% CI: 1.39-4.29). Subjects that smoked tobacco up to at least onset of treatment have 2.5 folds odds higher of being retreated than controls (cOR 2.5; 95% CI: 1.42-4.26). Other statistically significant exposures were being resident in ≥5 km away from clinic (cOR 2.6; 95% CI: 1.12-6.16), ever smoked ≥11 cigarettes per day (cOR 3.2; 95% CI: 1.29-7.75) and alcoholism (cOR 3.1; 95% CI: 1.19-7.92).

Among the retreatment and controls, there was no statistically significant association found with age (≥41 years / 15 – 40 years), marital status (married / single + divorced + widowed), possession of a minimum of secondary education (yes / no), daily transport fare to clinic (≥₦500 / <₦500) and cooking method in household (firewood + charcoal / kerosene stove).

4.5. Association between retreatment and adherence factors

Table 11: Association between retreatment and adherence (drug and follow-up) factors

Factor	Cases (n = 81)	Controls (n =162)	Crude OR	95% CI: LL, UL	P value
Ever missed clinic:					
Yes	31	35	2.25	1.25, 4.03	0.009
No	50	127			
Clinic days missed in intensive phase†:					
≥14 days	1	1	2.01	0.03, 158.9	1.110
<14 days	80	161			
Ever missed anti-TB doses:					
Yes	32	36	2.29	1.28, 4.08	0.007
No	49	126			
Cumulative anti-TB doses missed†:					
≥14 doses	1	1	2.01	0.03, 158.9	1.110
<14 doses	80	161			
In clinic & anti-TB drugs out of stock†:					
Yes	2	1	4.08	0.21, 241.9	0.517
No	79	161			
Health worker relationship with patient†:					
Poor	5	2	5.26	0.83, 56.04	0.086
Good	76	160			
Used adherence measures:					
Yes	58	137	0.46	0.24, 0.88	0.026
No	23	25			
Concurrently used other drugs:					
Yes	31	37	2.09	1.17, 3.74	0.018
No	50	125			
Concurrently used herbal preparations:					
Yes	11	18	1.26	0.56, 2.81	0.726
No	70	144			
Waiting room availability:					
Unavailable	27	39	1.58	0.88, 2.83	0.168
Available	54	123			
Seats availability:					
Unavailable	8	9	1.86	0.69, 5.02	0.330
Available	73	153			

†Fisher exact test used as cell frequency <5

Table 11 Summary: Association between retreatment and adherence to treatment

Subjects that ever missed clinic dates have 2-folds odds higher for being retreated compared to controls (cOR 2.3; 95% CI: 1.25-4.03). Likewise higher odds were found among the retreatment group than controls that ever missed anti-TB doses (cOR 2.3; 95% CI: 1.28-4.08) and concurrently used other drugs (cOR 2.1; 95% CI: 1.17-3.74). The used of adherence measures was however protective against retreatment (cOR 0.46; 95% CI: 0.24-0.88).

Among the retreatment and controls, there was no statistically significant association found with any of these exposures- missed clinic in intensive phase (≥14 days / < 14 days), missed doses of anti-TB (≥14 doses / < 14 doses), drugs out of stock while in clinic (yes / no), concurrently used herbal preparations (yes / no), health worker relationship with patient (poor / good), waiting room availability in the DOTS clinic (unavailable / available), and seats availability in the DOTS clinic (unavailable / available).

4.6. Association between retreatment and TB extent and comorbidity

Table 12: Association between retreatment and TB extent and comorbidity

Factor	Cases (n = 81)	Controls (n =162)	Crude OR	95% CI: LL, UL	P value
AFB smear grading at diagnosis:					
+ + +	27	43	1.38	0.78, 2.47	0.341
+ +/+/scanty	54	119			
AFB smear status at 3rd month*:					
Positive	13	26	2.06	0.96, 4.44	0.097
Negative	33	136			
Body mass index at diagnosis at diagnosis:					
<18.5 kg/m^2	44	86	1.05	0.62, 1.79	0.964
≥18.5 kg/m^2	37	76			
Serious drug side effects:					
Yes	19	25	1.68	0.86, 3.27	0.176
No	62	137			
HIV positive:					
Yes	27	33	1.95	1.07, 3.56	0.040
No	54	129			
Diabetes mellitus (DM) status†:					
Yes	4	3	2.75	0.45, 19.2	0.340
No	77	159			
Fasting blood sugar in DM range†:					
≥7.0 mmol/l	3	4	1.52	0.22, 9.20	0.859
<7.0 mmol/l	78	158			
Fasting blood sugar in pre-DM range:					
≥6.1 mmol/l	15	18	1.82	0.86, 3.83	0.164
<6.0 mmol/l	66	144			
Comorbid chronic lung disease status‡:					
Asthma	0	1	‡	‡	‡
Nil	81	161			

*Only documented

†Fisher exact test used as cell frequency <5

‡ Cells not computed because one of the values is zero

Table 12 Summary: Association between PTB retreatment and disease extent/comorbidity

TB/HIV comorbidity has odds of almost two folds higher among the TB retreatment group compared to controls (cOR 1.95; 95% CI: 1.07-3.56).

Among the retreatment and control group, there was no statistically significant association found with any of these exposures- pretreatment AFB smear density (3^+ / $<3^+$), AFB smear positivity status at 3rd month (positive / negative), pretreatment body mass index (<18.5 kg/m^2 / ≥18.5 kg/m^2), TB/DM comorbidity (yes / no), fasting blood sugar in diabetes range (≥7.0 mmol/l / <7.0 mmol/l), fasting blood sugar in pre-diabetes range (≥6.1 mmol/l / <6.1 mmol/l), and comorbid chronic lung disease status including asthma (present / absent).

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4.7. Independent predictors of PTB retreatment

Table 13: Independent predictors for PTB retreatment

Factor	Crude		Adjusted	
	OR (95% CI: LL, UL)	P value	OR (95% CI: LL, UL)	P value
Age in years (≥40 / 15 – 40)	1.55 (0.84, 2.87)	0.215		
Gender (Male/Female)	2.10 (1.13, 3.92)	0.027		
Highest education level attained (Below secondary / Above secondary)	1.26 (0.73, 2.18)	0.484		
Employment Status (Unemployed/Employed)	1.42(0.76, 2.67)	0.350		
Distance, house to clinic (5+ km/<5 km)	2.62 (1.12, 6.16)	0.04	3.69 (1.38, 9.90)	0.009
Ever smoked tobacco (Yes / No)	2.46 (1.42, 4.26)	0.002		
Quantity of tobacco ever smoked daily (≥11cigarettes / <11cigarettes)	3.16 (1.29, 7.75)	0.019	3.21 (1.18, 8.71)	0.022
Ever consumed alcohol (Yes / No)	2.44 (1.39, 4.29)	0.003		
Alcoholism assessed by CAGE tool (≥2 points / <2 points)	3.07 (1.19, 7.92)	0.033		
Ever discriminated against by people (Yes / No)	2.20 (1.17, 4.16)	0.021		
Score for overall knowledge (<69.97% / ≥69.97%)*	1.64 (0.95, 2.84)	0.099		
Score for causative agent (<80.74% / ≥80.74%)*	1.98 (1.05, 3.74)	0.049		
Score for overall attitude (<47.22% / ≥47.22%)*	1.71 (0.98, 2.98)	0.074		
Score for measures to improve health while on anti-TB (<42.47% / ≥42.47%)*	1.77 (1.01, 3.08)	0.059	2.28 (1.15, 4.52)	0.018
Ever missed clinic (Yes / No)	2.25 (1.25, 4.03)	0.009		
Ever missed anti-TB doses (Yes / No)	2.29 (1.28, 4.08)	0.007		
Health worker relationship with patient (Poor/Good)	5.26 (0.83, 56.04)	0.086		
Uses adherence measures (Yes / No)	0.46 (0.24, 0.88)	0.026	0.37 (0.17, 0.78)	0.009
Concurrently used other drugs (Yes / No)	2.09 (1.17, 3.74)	0.018		
Documented AFB smear status at 3rd month (Positive/Negative)	2.06 (0.96, 4.44)	0.097		
HIV status (Positive / Negative)	1.95 (1.07, 3.56)	0.040	2.49 (1.23, 5.06)	0.011

*Reference to its mean score

Table 13 Summary: Independent predictors for TB retreatment

Independent predictors identified after confounders were simultaneously controlled for during unconditional multiple logistic regression were distance ≥5 km from house to clinic [adjusted odds ratio (aOR) 3.69; 95% CI: 1.38-9.90], ever smoking ≥11 cigarettes daily (aOR 3.21; 95% CI: 1.18-8.71), negative attitude on measures to improving health while on anti-TB (aOR 2.28; 95% CI: 1.15-4.52), TB/HIV comorbidity (aOR 2.49; 95% CI: 1.23-5.06) and use of social support/adherence measures (aOR 0.37; 95% CI: 0.17-0.78).

CHAPTER FIVE: DISCUSSSION

With the view of assigning responsibility, factors identified were discussed under two major groups: health facility-based and patient-based factors.

5.1. Health facility-based factors

5.1.1. Clinic proximity

It was found that clinics located in a distance of ≥5 km away from the residence of patients had odds of 3.7 times higher in the retreatment group compared to controls (aOR 3.69; 95% CI: 1.38-9.90). Patients in such locations are likely to miss appointment dates due to long distance of travel.

Several studies reported that DOTS clinics located at a distance ≥5 km from residence put patients at increased risk of retreatment through initial default or treatment failure. Supportive studies to this are those conducted by Shargie and Lindtjørn 2007 in Southern Ethiopia[34], Namukwaya et al 2011 in Uganda[35] and Boateng et al 2010 in Ghana.[36] On the contrary, Erhabor et al 2003 in Ife did not find association between distance and TB treatment compliance.[37] Similarly, Amoran et al 2011 in Ogun did not find association between distance and TB retreatment after initial default.[25] but in a another study in Ogun, Amoran showed that DOTS centres located in a distance >10 km away from residence have about 7 times risk of retreatment through treatment failure.[38] In Plateau, Luka et al in 2011 also documented increased risk of retreatment through initial default among patients residing at a distance ≥5 km from clinic.[26]

5.1.2. Anti-TB drugs supply and availability in the clinic

Universal access to high-quality drugs is central to the Global Plan to Stop TB. The Global Drug Facility (GDF) is the frontline agent concerned with supply of affordable, quality-assured anti-TB drugs to countries in need.[56] In our study we did not find statistically significant association between retreatment and drug unavailability in the clinic, but it is worth noting that interrupted drug supply especially in the intensive phase increases patients risk for retreatment. In Zambia, Kaona et al 2004 reported that shortage of anti-TB drugs increases chances of non-compliance to treatment in TB patients.[59] Drug unavailability has also been shown by Kandel et al 2008 in South Africa[60] and by Ayisi et al 2011 in Kenya[61] as one of the reasons why patients interrupt or default their treatment. In University of Maiduguri Teaching Hospital, Nigeria, Yakubu et al 2012 reported that high TB treatment success rate was recorded in the hospital due to continuous supply of anti-TB drugs to patients.[63]

5.1.3. Social support and health worker relationship with patients

Our finding shows that the used of social support and other adherence measures, introduced to patients by the health facility, independently protects patients against the risk of being retreated by 63% (aOR 0.37; 95% CI: 0.17-0.78). This corroborates studies reported by Xu et al 2009 in China[40] where they found that regular home visitation to patients by health workers independently reduces risk of non-adherence by 77% (aOR 0.23; 95% CI: 0.10-0.51). In Bangladesh, Tasnim et al 2012 found that about 95.4% of TB patients utilized family social support to improve treatment success.[41] Boateng et al 2010 in Ghana[36] showed that introduction and use of family support independently protects against defaulting treatment by 71% (aOR 0.29; 95% CI 0.14-0.59).

In our findings, there was no statistically significant association between retreatment and health workers relationship status and availability of seats and waiting room in the DOTS clinics. However, very high proportion of the patients opined that health workers related cordially with them (cases 93.8% and controls 98.8%). High proportion of patients also reported availability of seats (cases 90.1% and controls 94.4%) and waiting room (cases 66.7% and controls 75.9%) in the clinic. These factors can improve adherence to treatment thus reducing risk of retreatment.

Finlay et al 2012 in South Africa[19] found that poor health care worker attitude towards patients increases risk of default by 2 folds (new: aOR 2.1; 95% CI 1.1-4.4). In Ethiopia, Gebremariam et al 2010 in an in-depth interview found lack of social support from health workers and families to be barriers to treatment adherence in TB/HIV comorbidity.[42] In Enugu, Nigeria Okeibunor et al 2007 found that about 25% of TB patients had complacent attitude in utilizing DOTS services due to reported poor health worker relationship with the patients.[81]

5.2. Patient-based factors

5.1.1. Age and Gender

Result shows that males have two folds odds higher for being retreated of PTB compared to controls (cOR 2.1; 95% CI: 1.13-3.92). Result is consistent with a study reported by Dooley et al 2011 in Morocco[14] where they found male gender to be an independent risk factor for retreatment (aOR 2.29; 95% CI: 1.10-4.77). Result also agrees with studies reported by Garrido et al 2012 in Brazil and Muture et al 2011 in Kenya, where males had 1 – 2 fold risk of being retreated after initial treatment default.[17,18] In Sagamu, Nigeria, Daniel et al 2006 had similarly found males to have two-folds risk higher of being retreated after initial treatment default.[24] On

the contrary, studies conducted in 2011 by Amoran et al in Ogun and another by Luka et al in Plateau did not find association between gender and treatment default.[25,26]

However, no statistically significant difference found with ages ≥40 years (middle-aged adults + elderly) compared to ages 15 – 40 years (adolescents + young adult). This was not a surprise because majority of the retreated patients (71.6%) and controls (69.8%) were young adults (age 20 – 40 years) and similar. Garrido et al 2012 in Brazil[17] reported the elderly patients to have slight protection against retreatment by not defaulting treatment (aOR 0.98; 95% CI: 0.98-0.99). In South Africa, Akpabio and Villiers 2011[23] reported TB retreatment to be commoner among in age group 23 – 44 years. Luka et al in Plateau[26] however showed that TB patients age >35 years and those in age groups 16 – 30 years and 31 – 45 years had higher risk of default.

5.1.2. Employment status and poverty

Employment, as a means of livelihood is protective against diseases especially when income is adequate to take care of necessities of life. Unemployment was not statistically significant in the study. Nonetheless, result obtained by Mishra, et al 2005 in Nepal, found unemployment (aOR 9.2) and low income (aOR 5.4) as independent risk factor for poor treatment adherence, a precondition for retreatment.[27]

Similarly, Jakubowiak et al 2007 in Russia[28] reported unemployment as independent risk factor for retreatment (through treatment default) with a four folds odds compared to controls (aOR 4.44; 95% CI: 2.23-8.86). Other supportive studies are results reported by Yen et al 2012 in Taiwan[13] where unemployment was found to be a risk factor for retreatment. Salami and

Oluboyo 2003 in Ilorin, Nigeria[33] also reported unemployment to be a risk for retreatment through poor treatment compliance.

On the contrary, Soomro and Qazi 2009 in Pakistan[29] found employment as a risk factor for TB relapse. Bhagat and Gattani 2010 in India[30] also found employment to be risk factor for defaulting retreatment. Fatiregun et al 2009 in Ibadan Nigeria[31] equally found the employed patients with low income level of <₦15,000 to have poor treatment outcome, a precondition for retreatment. Luka et al 2011 in Plateau, Nigeria[26] also did not find association between treatment interruption and unemployment.

5.1.3. Stigma and discrimination

Stigma and discrimination isolates and delays patients from seeking medical help, and causes poor adherence to treatment with eventual need for retreatment. Discrimination against TB patients was found to have two folds odds higher among the retreated group compared to the controls (cOR 2.20; 95% CI: 1.17-4.16). Although it was eliminated during logistic regression, Gebremariam et al 2010 in Ethiopia[42] however found stigma and discrimination as a cause of poor treatment adherence. Similarly, Finlay et al 2012 in South Africa[19] reported stigma to independently increased risk of defaulting treatment by 2 folds (aOR 2.0; 95% CI: 1.3-3.0). Our finding is also supported by studies reported by Christopher and Bosede 2010 in Ekiti and by Abioye et al 2011 in Lagos. Christopher and Bosede reported discrimination against TB patients to prevent them from utilizing health services, thus increasing risk of retreatment.[32] Abioye et al reported stigma and discrimination to cause poor treatment adherence, which can lead to retreatment.[43]

5.1.4. Knowledge and attitude of patients

Knowledge is having conscious information (cognition) about a subject matter while attitude is 'feeling' or 'affect' that drives an individual towards an action. Referencing benchmark of 50%, overall knowledge score was satisfactory (mean, 69.97 ± 11.21%) with no statistically significant association between the retreated and control group. However, only 55.6% of the retreated patients and 67.3% of the controls scored above the overall mean knowledge score. The component mean knowledge scores recorded exceeded 70.0% except for knowledge about risk factors (mean score, 28.64 ± 21.03%) and preventive measures (mean score, 26.38 ± 20.33%). Statistically significant association was with knowledge on causative agent based on score below its mean 80.74% (cOR 1.98; 95% CI: 1.05-3.74). It was however noted that both the cases and controls scored satisfactorily very high marks about knowledge on causative agent (mean score 80.74%).

Vijay et al 2010 in India found poor TB knowledge to be risk factor for retreatment through treatment default.[52] In Uganda Obuku et al 2012 found satisfactory TB knowledge among TB patients in terms of disease curability and treatment, except in aspect of causative agent, clinical features, transmission, prevention, free treatment.[55]

Studies by Cramm et al 2010 in South Africa[53], Ngadaya et al 2009 in Tanzania[54] and Muture et al 2011 in Kenya[18] found that TB patients with unsatisfactory knowledge of TB have 8 times increased risk of retreatment after treatment default (OR 8.67; 95% CI: 1.47-51.3). In Ekiti, Christopher and Bosede 2010 also found TB patients to have satisfactory knowledge about the disease.[32] Works by Fatiregun et al 2009 in Ibadan[31] and by Luka et al 2011 in Plateau[26]

similarly reported poor knowledge about TB to be a risk factor for retreatment through default, relapse or failure.

In area of attitude, the component and overall mean attitude scores recorded were below the minimum benchmark of 50%. Only 34.6% of the retreated patients and 47.5% of the controls scored above the overall mean attitude score (47.22 ± 8.47%). %). Association between cases and controls did not achieve statistical significance except for attitude on measures to improve health while on anti-TB based on score below its mean 42.47% (aOR 2.28; 95% CI: 1.15 - 4.52). The below average assessment score suggests that TB patients have negative attitude towards the disease. Negative attitude is reported by studies of Jittimanee et al 2009 in Bangkok[39], Munro et al 2007[82], Xu et al 2009 in China[40] and Nkulu et al 2010 in Sweden.[83] Other studies that reported negative attitude are by Hashim et al 2005 in Iraq[84], Finlay et al in South Africa[19], Ayisi et al 2011in Kenya[61], and by Christopher and Bosede 2010 in Ekiti, Nigeria.[32] Positive attitude was however reported by Tasnim et al 2012 in Bangladesh.[41]

5.1.5. Exposure to tobacco and alcohol

The odds of smoking tobacco till at least the onset of treatment was higher in the retreatment group compared to the controls (cOR 2.5; 95% CI: 1.42-4.26). Furthermore, daily smoking of ≥11 cigarettes till at least the onset of treatment was an independent risk factor for retreatment (aOR 3.21; 95% CI: 1.18-8.71).

Supportive studies included Chiang et al 2012 in Taiwan[47] where smoking >20 cigarettes per day decreased odds of TB cure or treatment completion by 77% (OR 0.23; 95% CI: 0.05-0.98). Batista et al 2008 in Brazil[46] reported tobacco smoking to be an independent predictor of

retreatment (aOR 2.53; 95% CI 1.23-5.21). Dooley et al 2011 in Morocco[14] also obtained odds of substance use including tobacco to be almost 3 times in retreatment group compared to the controls (OR 2.73; 95% CI 1.04-7.15). In South Africa, studies by Mphothulo et al 2012 and Visser et al 2012 found smoking to be associated with poor treatment outcome, a precondition for retreatment.[50,51] Furthermore, Luka et al 2011 in Plateau Nigeria[26] (OR 2.02; 95% CI: 1.11-3.67) and Salami and Oluboyo 2003 in Ilorin[33] reported smoking to be associated with poor treatment outcome, a precondition for retreatment. On the contrary, Parikh et al 2012 in Mumbai India[15] did not find tobacco to be associated with retreatment through delay sputum conversion and likewise Jakubowiak et al 2007 in Russia[28] did not find association between tobacco smoking and retreatment through treatment default.

With regard to alcohol, the retreatment group had higher odds with for alcohol intake (cOR 2.4; 95% CI: 1.39-4.29) and alcoholism (cOR 3.1; 95% CI: 1.19-7.92). In agreement to this finding, WHO 2011 reported that harmful alcohol drinkers with TB disease have 2 – 8 relative risk of TB retreatment through treatment failure.[4] Lonnroth et al 2011 found that people who drink alcohol >40g/day have a 3 times increased risk of TB.[45] Furthermore, Marlucia da Silva Garrido et al 2012 in Brazil[17] documented that TB patients with alcohol drinking problem have 1.5 times increased risk of TB retreatment through treatment default (aOR 1.51; $p<0.001$). A cohort study by Sendagire et al in Uganda[49] similarly found daily alcohol consumption to be a predictor of TB treatment default (aOR 4.4; 95% CI: 1.8-13.5). Salami and Oluboyo 2003 in Ilorin[33] also found alcohol consumption to be associated with poor treatment outcome.

Psychoactive substances are used commonly among the young adults, 20 – 40 years, and this age group represented the greatest proportion of the subjects studied. It is important to note that,

tobacco and harmful alcohol consumption depresses immunity, delays wound healing and impair social and medical responsibilities. Users are at risk of non-adherence to treatment leading to retreatment through default, failure or relapse.

5.1.6. Adherence to treatment (drugs and follow-up) and adverse drug reaction

Adherence to drugs and follow-up visits are primary responsibility of patients to prevent retreatment. Additional drugs (pill burden) to manage comorbidity and ingestion of herbal preparations interfere with TB treatment. Result showed odds of 2.3 times higher for patients that ever missed clinic dates in the retreatment group compared to controls (cOR 2.3; 95% CI: 1.25-4.03). Patients that ever missed anti-TB doses also had similar odds ratio (cOR 2.29; 95% CI: 1.28-4.08). Result, supported by studies reported by Ai et al 2010 in China[57] (OR 8.7; 95% CI: 3.9-18.4). Vijay et al 2010 in India[52] also found that patients who missed anti-TB doses were independently at increased risk of retreatment through initial treatment default (aOR 2.56; 95% CI: 1.82-3.57). Similarly, Dooley et al 2011 in Morocco[14] found that patients that missed anti-TB doses in the intensive phase had higher odds of retreatment compared to controls (OR 10.9; 95% CI: 3.47-34.0). In contrast, studies by Anyama et al 2007 in Uganda[58] did not find association between retreatment and patients that ever missed anti-TB.

Result did not find statistically significant association between retreatment and patients that missed ≥14 doses of anti-TB or missed ≥14 days of clinic appointment dates. However, studies by Namukwaya et al 2011 in Uganda[35] reported patients who missed ≥14 doses of anti-TB (OR 3.3; 95% CI: 1.55-7.05) or missed ≥14 days of clinic appointment dates (OR 12.3; 95% CI: 4.55-33.34) to respectively have 3 and 12 folds odds of retreatment compared to controls.

Patients that concurrently used other drugs had a two-fold increased risk for retreatment even though it was eliminated during logistic regression (cOR 2.09; 95% CI: 1.17-3.74). Concurrent drug used is accounted for in the treatment of comorbidity or patients could have also concealed their use of herbal preparations or other drugs for personal reasons. However, there was no statistically significant association found between retreatment and used of herbal preparations. Concurrent drug use and herbal preparations for instance, reduce the potency and amplify side effects of anti-TB drugs. Nonetheless, Muture et al 2011 in Kenya[18] found herbal medication to be a risk factor for retreatment through treatment default (OR 5.7; 95% CI: 1.37-23.7). Christopher and Bosede 2010 in Ekiti, Nigeria[32] also found the use of unorthodox care among TB patients.

Adverse drug reactions increases risk for retreatment through non-adherence to medication. This was not found in this study same as how Namukwaya et al in 2011 in their study in Uganda did not find.[35] However, adverse drug reactions has been reported in China by Xu et al 2009[40], and by Ai et al 2010[57], and similarly in Ghana by Boateng et al 2010[36] (OR 3.0; 95% CI: 1.48-6.09).

5.1.7. TB/HIV comorbidity

TB/HIV comorbidity has about 2.5 folds odds higher among the retreated group compared to the controls (aOR 2.49; 95% CI: 1.23-5.06). HIV infection increases risk for recurrent TB, which may be due to either TB relapse or re-infection.[64,65] Concurrent treatment of TB/HIV can be complicated by factors such as overlapping drug toxicities, drug-drug interactions, pill burden and poor adherence to drugs. These situations further increase the risk for retreatment.

Finding on TB/HIV comorbidity corroborated reports by Garrido et al 2012 in Brazil[17] (aOR 1.62; P<0.0001), Muture et al 2011 in Kenya[18] (OR 1.56; 95% CI: 1.25-1.94), and by Arentz et al 2011 in Mombasa, Kenya[66](RR 4.61; 95% CI: 1.69-12.59). Burton et al 2011 in Ghana[67] (OR 2.4; 95% CI: 1.2-5.2) and Ige and Oladokun 2011 in Ibadan, Nigeria[70](OR 69.4; 95% CI: 9.4-512.9) also found TB/HIV co-infection to have a very high risk of retreatment through treatment failure. Alarming rate of TB/HIV comorbidity was also reported also reported by Ifebunandu et al 2012 in Nigeria.[69]

Contrary to our finding, association between retreatment and TB/HIV comorbidity was not found in studies conducted by Nyamogoba et al 2012 in Kenya[68], Mphothulo et al 2012 in South Africa[50] and Anyama et al 2007 in Uganda.[58] In Nigeria Jibrin et al in Gombe[71], Daniel et al 2006 in Sagamu[24] and Amoran in Ogun similarly did not find association between TB/HIV comorbidity and retreatment through initial treatment default.[25]

5.1.8. TB/Diabetes comorbidity

Association between retreatment and TB/DM comorbidity was not found in the study. This could have been altered by the dietary pattern in Adamawa state. Inhabitants of Adamawa state eat a

lot of Moringa oleifera (‘zogale’) leaves inform of soup or salad. The leaves are rich in many nutritional and therapeutic benefits one of which is blood glucose control in hyperglycaemic state.[85,86] It is important to note that patients with TB/DM comorbidity have higher risk of TB retreatment through relapse, failure or default. Systematic review by Baker et al 2011 shows a two-fold risk for retreatment in TB/DM comorbidity.[16]

CHAPTER SIX: CONCLUSION AND RECOMMENDATIONS

6.1. Conclusion

Determinants of retreatment with first line anti-TB drugs (FLADs) were investigated among smear positive patients in Adamawa state from 4th quarter 2012 to 2nd quarter 2013. Of 243 patients studied (81 cases, 162 controls), mean age 35.2 ± 11.7 years (cases 37.8 ± 10.6; controls 33.9 ± 12.0), 70.4% young adults 20 – 40 years (cases 71.6%; controls 69.8%), 69.1% males (cases 79.0%; controls 64.2%), 59.3% married (cases 56.8%; controls 60.5%), and 46.1% attained secondary education (cases 44.4%; controls 46.9%).

Determinants identified– knowledge on causative agent based on score below its mean 80.74% (cOR 1.98; 95% CI: 1.05-3.74) and attitude on measures to improve health while on anti-TB based on score below its mean 42.47% (cOR 1.77; 95% CI: 1.01-3.08). Male gender (cOR 2.1; 95% CI: 1.13-3.92), and clinic location ≥5 km from residence (cOR 2.6; 95% CI: 1.12-6.16). Smoked till at least onset of treatment (cOR 2.5; 95% CI: 1.42-4.26), daily smoking of ≥11 cigarettes till at least onset of treatment (cOR 3.2; 95% CI: 1.29-7.75), alcohol consumption till at least onset of treatment (cOR 2.4; 95% CI: 1.39-4.29) and alcoholism (cOR 3.1; 95% CI: 1.19-7.92). Ever discriminated against (cOR 2.2; 95% CI: 1.17-4.16), ever missed clinic (cOR 2.3; 95% CI: 1.25-4.03), ever missed anti-TB doses (cOR 2.3; 95% CI: 1.28-4.08), TB/HIV comorbidity (cOR 1.95; 95% CI: 1.07-3.56), concurrent drug use (cOR 2.1; 95% CI: 1.17-3.74) and used of social support and adherence measures (cOR 0.46; 95% CI: 0.24-0.88).

Independent predictors identified were distance ≥5 km from house to clinic (aOR 3.69; 95% CI: 1.38-9.90), ever smoking ≥11 cigarettes daily (aOR 3.21; 95% CI: 1.18-8.71), negative attitude on measures to improving health while on anti-TB (aOR 2.28; 95% CI: 1.15-4.52), TB/HIV

comorbidity (aOR 2.49; 95% CI: 1.23-5.06) and use of social support/adherence measures (aOR 0.37; 95% CI: 0.17-0.78).

Based on independent predictors identified, the State and Local Government Areas are recommended to site clinics closer at distances of <5 km from homes, introduce tobacco dependence and cessation programme in clinics, closely monitor TB/HIV comorbidity, promote healthy measures to improving health while on anti-TB and reinforce social support and other adherence measures.

6.2. Recommendations

6.2.1. Major recommendations

Major recommendations to the state and Local Government Areas were based on independent predictors identified.

1. The state and LGAs, requested to site functional clinics at distances of less than 5 km from homes.
2. The state and LGAs, requested to introduce tobacco dependence and cessation programme in DOTS clinics.
3. The state and LGAs, requested to draw attention of anti-TB drug prescribers on the need to monitor TB/HIV comorbidity closely as they stand the risk of retreatment from drug-drug interactions, pill burden and overlapping drug toxicities.
4. The state and LGAs in collaboration with stakeholders like the community-based organizations and faith-based organizations are requested to promote healthy measures to improving patients' health while on anti-TB and reinforce social support and adherence

measures consistently. The adherence social support includes family members, community volunteers, patient-patient network, health worker-patient network and use of alarm clocks.

6.2.2. Other recommendations

Other recommendations to the state and Local Government Areas were based on factors eliminated during multiple logistic regression analysis.

1. The state and LGAs, requested to introduce alcohol dependence and cessation programme in DOTS clinics.
2. The state and LGAs, requested to update on regular basis knowledge of anti-TB drug prescribers about concurrent drug use and to probe concurrent drug use by patients during treatment as this may reduce potency of anti-TB drugs or cause adverse drug reactions.
3. The state and LGAs in collaboration with stakeholders like the community-based organizations and faith-based organizations are requested to carry out continuous patient education on the need to adhere to treatment and sensitize the public on the need to show love, care, empathy and support to TB patients as this will prevent discrimination and prejudice attached to the disease.

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Appendix 1: Consent form in Hausa Language

Gabatarwa:

Gaisuwa tare da fatan alheri. Suna na Dr. MALAU MANGAI, likitan lafiya daga Jamiyar kiwon lafiya ta Ahmadu Bello University Zaria da hukumar kiwon lafiya ta Najeriya. Masu jagora da horaceni a wanan binchike sune Dr. M. Nasir Sambo (08033023531) da kuma Prof. K. Sabitu (08037037647) daga Jamiyar kiwon lafiya ta Ahmadu Bello University Zaria.

Ina bukatar darajar izini daga gare ka/ki domin in yi ma ka/ki wasu tambayoyi game da cutar tarin fuka (wato tuberculosis a turance) da kuma yanda a ke kiyaye wana cutar a jihar Adamawa. Domin wanan aiki, na karbi izini daga hukumar kiwon lafiya ta jihar Adamawa.

Game da tambayoyin, baza a bukaci sunan ka/ki ba domin a tsare daraja da kuma asirin kowa. Yardawan ka/ki a cikin wanan binchiki ba tilas bane, amma yardawa da kuma izinin ka/ki zai taimaka kwarai domin za a yi amfani da sakamakon wanan binchiki a fanin kiyaye cutar tarin fuka a jihar Adamawa da kewayenta.

A cikin wanan tambayoyin, za a yi awun nauyi, tsayi da jini domin a gane koshin lafiyar ka/ki. Wadanan gwaji za a yi su a kyauta ba tare da kudi ba. Nagode domin goyon baya da kuma lokacin da ka/ki bani. Ina sake tabatar ma ka/ki da cewa ansoshin ka/ki a asirche su ke, baza a gaya wa wani ba.

Na amince ☐ **Ban amince ba** ☐

Idan ka/ki amince:

Suna……..Kwanar wata…….

Ko ka/ki dangwala babban dan yatsa na dama.

Suna maisheda…….Kwanar wata……

Ko ka/ki dangwala babban dan yatsa na dama.

Appendix 2: Consent form in English

Introduction:

Dear sir/ma, I am a resident of the Nigeria Field Epidemiology and Laboratory Training Programme, Ahmadu Bello University (ABU) Zaria and Federal Ministry of Health. My supervisors are Dr. M. Nasir Sambo (08033023531) and Prof. K. Sabitu (08037037647) from ABU Zaria.

I seek your kind permission to administer you this questionnaire prepared to find out some risk factors for retreatment of tuberculosis in Adamawa state. I assure you that results from this study will not carry people's name for the purpose of confidentiality. Findings will however be used to improve on the prevention, control and treatment of tuberculosis in the state.

Your selection to participate in this study is optional. This study has obtained clearance from the Research and Ethical Committee Adamawa SMOH. You may also be required to have your weight, height and blood examined to assess your health condition and this is will be done free of charge. I appreciate the time you will spend in responding to these questions and sincerely assure you again of strict confidentiality.

Thank you for your cooperation.

I agree ☐ **I do not agree** ☐

Name of patient…….Date…….

Name of witness ……Date……

Appendix 3: Questionnaire modified from the Ugandan studies[35,58]

Patient Identification Code

Questionnaire number…… Phone number……

Date of interview (dd/mm/yyyy)……

A. Patient registration status

1. Did you take anti-TB drugs for at least 1 month in the past before this current treatment?

   Yes (i.e. retreatment for TB) ☐ No (i.e. new case of TB) ☐

   If yes, date……. duration in weeks……

2. Date Pulmonary Tuberculosis (PTB) diagnosed (check treatment card)…….
3. Date current anti-TB drug started (check treatment card)……
4. Anti-TB regimen currently on (check treatment card)…….

B. Demographic Factors

5. Place of residence: LGA:……. Community:……
6. Date of birth (dd/mm/yyyy):……
7. Sex: Male ☐ Female ☐
8. Marital status: Single ☐ Married ☐ Divorce ☐ Widowed ☐
9. Occupation(s):……
10. Tribe:……..
11. Religion: Islam ☐ Christianity ☐ Traditional ☐ Others (specify)……..
12. Educational level: Nil ☐ Primary ☐ Secondary ☐ Tertiary ☐ Koranic ☐

    Others (specify)……

C. Socioeconomic Factors

13. **a)** Which method of cooking does your household use most of the time?

    Firewood ☐ Charcoal ☐ Animal dung ☐ Kerosene stove ☐ Electric/gas cooker ☐

    b) What is the nature of the cooking environment? Open ☐ closed ☐

14. Average amount spent each day on transport from house to DOTS centre

    <₦200 ☐ ₦200 – <₦500 ☐ ₦500 – <₦1,000 ☐ >₦1,000 ☐

15. Your income status since TB diagnosed: No change ☐ Reduced ☐ Increased ☐

16. What is your usual means of transportation to the DOTS clinic?

Foot☐ Bicycle☐ Motorcycle☐ Vehicle ☐ Others (specify)…….

17. Average distance from your house to the DOTS clinic.

1 – 2 km ☐ 3 – 4 km ☐ ≥5 km ☐

18. Using your usual means of transportation, time duration it takes you get to the DOTS clinic.

< 30 minutes ☐ 30 minutes – 1 hr ☐ > 1 hr ☐

19. How long do you have to wait at the DOTS clinic before you are attended to?

< 1hr ☐ 1- 2hrs ☐ 3 – 4 hrs ☐ > 4hrs ☐

20. Have you ever missed clinic appointments? Yes ☐ No ☐

If yes, number of times you missed in: intensive phase…….. Continuation phase…….

Give reason…….

21. Have you ever missed your anti-TB doses? Yes ☐ No ☐

If yes, number of times you missed doses in: Intensive phase……. Continuation phase……

Give reason…….

22. Are there measures you take so that you do not miss your anti-TB drugs? Yes ☐ No ☐

If yes, which measures?.....

23. Have you ever visited DOTS clinic on your appointment date and was told by a healthcare worker to come back next time because drugs were not available?

Yes ☐ No ☐

If yes, number of times with dates? Intensive phase…….. Continuation phase…….

24. Have you ever withdrawn yourself from friends, relations or public because of shame due to this illness? Yes ☐ No ☐

25. Have friends, relations or public because of this illness ever discriminated upon you?

Yes ☐ No ☐

26. How can you rate the way health workers relate with you in the DOTS clinic?

Good ☐ Very good ☐ Poor ☐ Very poor ☐

27. Where do you seat to wait for your turn each time you visit DOTS clinic?

Outside without seats ☐ Outside with seats ☐

Waiting room without seats ☐ Waiting room with seats ☐

28. Would you prefer to be treated for the TB elsewhere? Yes ☐ No ☐

If yes, place of preference…….. Reason……

29. Before this illness, were you in close contact or living in the same house with someone coughing and on TB treatment? Yes ☐ No ☐

30. Tobacco use status: Currently use it ☐ Used it in the past ☐ Never used it ☐

For current tobacco users (Question 30 – 32):

31. Date you started using tobacco?.....

32. Method of tobacco use (choose all that applied)

Smoking ☐ Chewing ☐ Sniffing ☐ Others (specify)……

33. Average quantity of tobacco you use per day.

S/N	Name of brand/type	Average number per day
1		
2		

For past tobacco users (Question 34–36)

34. Date started using tobacco before you quitted……

35. Date you quitted tobacco……

36. Reason for quitting…….

Past tobacco users & those who never used tobacco (Question 37–38)

37. On an average, how many minutes or hours per day do you spend where someone/people smoke?.....

38. Is/are there member(s) of your household who smokes? Yes ☐ No ☐

39. Alcohol use status:

Currently drink alcohol ☐ Drank alcohol in the past ☐ Never drank alcohol ☐

For current alcohol drinkers (Question 40–43)

40. Date you started drinking alcohol.....

41. Reflect in a typical month, how often do you drink alcohol in a week?

1 – 2 days ☐ 3 – 4 days ☐ 5 – 7 days ☐

42. Reflect in a typical month, average number of alcoholic beverage you usually drink per day

S/N	Brand/type	Average number of alcoholic beverage drink per day
1		
2		

43. **CAGE Assessment for Alcohol Abuse**

CAGE characteristic	Yes	No
Have you felt the need to ***Cut down*** on your drinking?		
Do you feel ***Annoyed*** by people complaining about your drinking?		
Do you ever feel ***Guilty*** about your drinking?		
Do you ever drink an ***Eye-opener*** in the morning to relieve shakes?		

For past alcohol drinkers only (Question 43–45)

44. Date you started drinking alcohol before you quitted.....

45. Date you quitted alcohol.....

46. Reason for quitting……..

D. Past Medical History

47. Experienced any serious side effect(s) with the TB drugs? Yes ☐ No ☐

If yes, what did you do initially?.....

List the side effects and date…….

48. Is there treatment support group in your DOTS centre? Yes ☐ No ☐

49. Have you ever been told by a doctor/health worker that you have diabetes mellitus?

Yes ☐ No ☐

If yes, when was the diabetes diagnosed?.....

50. Have you ever been told by a doctor/health worker that you have HIV? Yes ☐ No ☐

If yes, when was the HIV diagnosed?.....

51. Have you ever been told by a doctor/health worker that you have any other illness apart from the ones I had asked you above? Yes ☐ No ☐

If yes: Name of illness……..... Date of diagnosis of the illness?.....

52. Underwent any surgical operation/procedure in the course of illness? Yes ☐ No ☐

If yes, name of procedure…… date……

53. Concurrent use of other drugs apart from the anti-TB drugs? Yes ☐ No ☐

54. Concurrent ingestion of herbal preparations/unorthodox medication? Yes ☐ No ☐

E. Physical Examination and Laboratory diagnosis/screening

55. Sputum smear microscopy for diagnosis and follow up **(check treatment card)**

Month	Date sputum collected	Sputum specimen	Positive				Negative	Not done
			3+	2+	1+	Scanty (1–9 bacilli/100 hpf)		
0 (at diagnosis)		1						
		2						
		3						
2								
3								
5								
7								

56. Sputum culture done? **(check treatment card)** Yes ☐ No ☐

If Yes, record result

Month	Date	Result
0 (at diagnosis)		
2		
3		
5		
7		

57. Baseline drug susceptibility (sensitivity) testing done? Yes ☐ No ☐

If Yes, record date (dd/mm/yyyy)……. and result below

Isoniazid (H)	Rifampicin (R)	Pyrazinamide (Z)	Ethambutol (E)	Streptomycin (E)

58. Chest X-Ray (CXR) done at diagnosis? Yes ☐ No ☐

Date done	CXR	Reported as:			Not reported
		Normal	abnormal and:		
			suggestive of PTB (if there are cavities indicate)	not suggestive of PTB	
	1				
	2				
	3				

59. BCG scar? Present ☐ Absent ☐

60. Weight/height at diagnosis and on follow up **(check treatment card)**

Month	Date	Weight (kg)	Height (m)
0 (at diagnosis)			
2			
3			
5			
7			

61. HIV status? Positive ☐ Negative ☐

62. Fasting Blood Glucose (mmol/l)…….

F. Knowledge, Attitude and Practice

63. What is the cause of tuberculosis (TB) of the lungs?.....

64. How can someone be infected with the agent that causes TB of the lungs?.....

65. What are the conditions, situations or illnesses that can put someone at risk of developing TB?……..……

……..…….

66. Mention common symptoms/signs that can make you suspect someone of having TB?…….....

.....……..

67. How can TB be prevented?……..…….……

68. Is TB curable/treatable? Yes ☐ No ☐

If yes, how can it be cured/treated?.....……

69. For how long can a patient be on anti-TB drugs?

a) For initial treatment with first line anti-TB……

b) For retreatment with first line anti-TB ……..…..

70. Are there consequences of not completing TB treatment? Yes ☐ No ☐

If yes, mention the consequences of not completing TB treatment…….

……..

71. What advices will you give to someone you suspect has TB?……

72. What advices will you give to someone placed on anti-TB drugs?

……

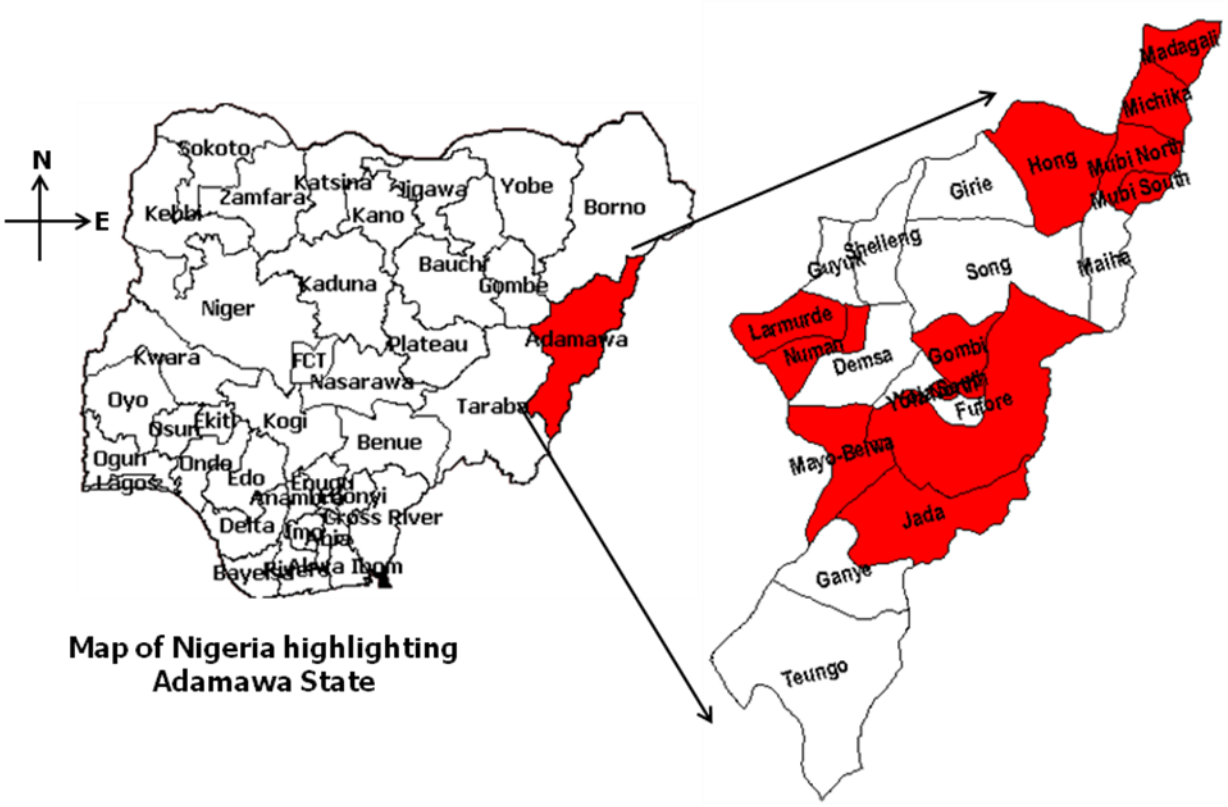
……..……

73. What are the things you do to improve your health since you started anti-TB drugs?

……

……..…….

Appendix 4: Map of study area in Adamawa state



Map of Nigeria highlighting Adamawa State

Map of Adamawa State highlighting Lamurde, Numan, Mayo-Belwa, Jada, Fufore, Yola South, Gombi, Hong, Mubi South, Mubi North, Michika & Madagali LGAs

Appendix 5: Ethical clearance approval