Factors related to poor tuberculosis treatment outcome in Jimma university specialized hospital: A prospective cohort study.

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Abstract

Background - Tuberculosis has been one of the major causes of morbidity and mortality in Ethiopia for long. Treatment outcome of tuberculosis is sub optimal nationally. An understanding of the factors predisposing to poor outcome may allow the development of adjunctive treatment strategies or closer clinical monitoring in high-risk individual.

Objective – The main objective of the study was to describe the outcomes of tuberculosis treatment and to identify factors associated with poor treatment outcome.

Methods and Materials - A prospective cohort study was conducted on all tuberculosis patients between November 2013 and September 2014 E.C. Data was cleaned, edited and entered to SPSS window version 16.0 for analysis. The strength of correlation between variables was tested by logistic regression analysis. The values of $p< 0.05$ were considered statistically significant. The results are depicted with tables and figures.

Results - A total of 193 tuberculosis patients with pulmonary(61.2%) and extrapulmonary (38.8%) tuberculosis were involved in the study with a median age of 26$\pm$ 12. The rate of unsuccessful treatment outcome was 11.4 %. HIV co-infection (OR 21.88 p-0.00) and meningeal involvement (OR 4.77 p-0.05) significantly increase poor treatment outcome.

Conclusion and Recommendation – HIV co-infection and meningeal involvement increases rate of poor outcome. Such patients demand close follow up and further study is recommended to find out and solve the factors behind poor outcome in these group.

Budget and Project Time- Project was conducted by the finance from CBE office of Jimma University between November 2013 and April 2014E.C

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Acronyms and Abbreviations

TB –Tuberculosis

EQA – External quality assurance

DOTS - Directly Observed Chemotherapy Short Course

WHO – World health organization

HIV – Human immune deficiency virus

MDR – multi drug resistance

AOR- Adjusted odds ratio

HR – Hazard ratio

JUSH – Jimma University specialized hospital

COR – crude odds ratio

CBE – community based education

Chapter 1. Introduction

1.1 Background

Mycobacterium Tuberculosis has been present in the human population since antiquity fragments of the spinal column of Egyptian mummies in 2400 B.C. showed definite pathological signs of tubercular decay. In 1882, the bacterium was seen and identified by the aided human eye for the first time. But the most important breakthrough came in 1944 when streptomycin successfully, and very quickly, cured a critically ill patient (1, 2).

Inhalation is the commonest mode of transmission. It commonly involves the lungs in immunocompetent patients with other organ involvement of around 20%. But in immunocompromised, extra pulmonary involvement can reach up to two third of cases. Involvement of the brain is the most serious with a universal mortality if untreated and 25% neurologic sequelae in treated patients. The overall mortality of untreated pulmonary tuberculosis within three years is 50% and 50–65% within 5 years (2, 3).

Diagnosis of tuberculosis is commonly made by taking history, physical exam and some laboratory tests. Sub acute productive cough with an intermittent fever and significant weight loss is usual patient presentation. The most common method for diagnosing TB worldwide is sputum smear microscopy (developed more than 100 years ago), in which bacteria are observed in sputum samples examined under a microscope. In countries with more developed laboratory capacity, cases of TB may also be diagnosed via culture methods (the current gold standard) or, using rapid molecular tests. Sputum smear is positive in 80% in immunocompetent individuals in EQA certified laboratories.
Streptomycin was the first effective anti-TB drug introduce in 1944. Since then due advances were made. Directly Observed Chemotherapy Short Course (DOTS) strategy was developed by the WHO, with the objective of achieving success rate of 85% and case detection of 70% by the year 2015 (3).

The evaluation of outcome of anti-tuberculosis treatment is one of the major indicators for the assessment of the performance of a national TB program (who stop2012). WHO considers tuberculosis treatment success if outcome is cure or treatment completed. Other possible

outcomes are failure, default, death and not evaluated for a patient whose treatment outcome is not known. While the national Tuberculosis, Leprosy and TB/HIV Prevention and Control Program of Ethiopia avoids the term not evaluated.

Patients with tuberculosis who are seriously ill to be sent home and those with life threatening complication are usually admitted to a hospital setup specialized for TB care.

1.2 Statement of the problem

Tuberculosis is the leading cause of outpatient visit, hospital admission and inpatient morbidity and mortality only second to malaria in Ethiopia; of course in sub-Saharan Africa. The incidence prevalence and mortality from tuberculosis in Ethiopia is far devastating than the rest of the world. Incidence and prevalence rates were more than twice the global value in 2009. Mortality rates despite standard treatment is 18/100,000 worldwide, 23 in high burden countries and 42/100,000 in Ethiopia. (3)

Different factors are incriminated to augment unsuccessful treatment outcome of active tuberculosis. HIV co infection and MDR tuberculosis were listed on top in different studies. Studies done in different parts of the world mentioned late presentation, co morbidity, low admission hemoglobin, old age, male sex and extensive parenchymal lesion as important causes of death in tuberculosis patients.

Rate of MDR in new and retreatment groups in Ethiopia is far lower than the global or the high burden countries especially in new patients. (3)

Presence of such a high rate unsuccessful treatment outcome despite proper DOTS implementation and in the absence of exaggerated drug resistance pattern asks an additional agent for proper explanation. In our setting such amendable factors presence cannot be left without a question and sorting them out and developing strategy to tackle this issues would definitely open window for better survival and decreased mortality in TB patients.

Chapter 2. LITRATURE REVIEW

Many has been said, written and done on tuberculosis, an old friend, but it still is among the leading cause of death worldwide. A Russian young man described his inevitable death by saying “it is not romantic to die with tuberculosis in 20th century”. Of course it doesn’t sense good to die from such disease. There were 8.8 million cases of Tb worldwide with more than 1.4 million deaths in 2010, global death rates being more than 15. It is sure that incidence and mortality are decreasing since 2000. Except the WHO Africa region all others will achieve the 50% mortality reduction in 2015. (3, 4)

In 2010 the global success rate of tuberculosis treatment was 85% though it was not homogenously distributed. The highest success rate was recorded in western pacific region rate being 92%. Africa has the lowest success rate 73 %.(3)

Europe, across the whole Region, 9.0% of cases was reported as failed treatment, 8.4% died, and 6.9% defaulted. A study done in Finland to asses treatment outcome among 629 patients a favorable outcome was achieved in 441 (70.1%), 17.2% (108) died and other unfavorable outcome took place in 12.7% (80). Significant independent risk factors for death were male sex, high age, non-HIV -related immunosuppression and any other than a pulmonary specialty being responsible for stopping treatment. History of previous tuberculosis was inversely associated with the risk of death (5, 6).

In a similar study in Spain on 1490 patients the treatment outcomes were: cured 792 (53.2%), completed treatment 540 (36.2%), failure 2 (0.1%), transfer-out 33 (2.2%), default 27 (1.8%), death 27 (1.8%), lost to follow-up 65 (4.4%), other 4 (0.3%). Age above 50 and HIV infection were significant risk factors for death. In this study living alone and injection drug use were among the risk factors associated with non adherence. (7)

A retrospective study in Gambia, West Africa, intended to determining the outcome of treatment of adult with smear-positive tuberculosis showed that high bacterial load and smear positivity at end of two months of chemotherapy were associated with defaulting later during treatment.

patients with a poor patients provider interaction and those who change residence were at risk for default in a south African case control study. In Morocco Independent risk factors for failure, default, or early relapse after initial treatment included male gender (aOR = 2.29, 95% CI 1.10-4.77), positive sputum smear after 3 months of treatment (OR 7.14, 95% CI 4.04-13.2), and hospitalization (OR 2.09, 95% CI 1.01-4.34). Higher weight at treatment initiation was protective. (8, 9)

Alcoholism has been identified as an important predictor of treatment default in several continents. In India, the aOR was 1.72 ($p = 0.002$), in Russia, 1.99 ($p = 0.04$), in Africa, 4.97 ($p = 0.01$) and in Asia, 6.01 (95% CI 1.68 – 19:47). In Brazil, a study revealed that people who reported use of alcohol had a 51% greater risk for treatment default ($p<0.001$) when compared to those who reported not using alcohol. The abuse of alcohol combined with antituberculosis drugs increases the risk of liver damage. (10, 11, 12, 13, 14)

Passive or active exposure to tobacco smoke is significantly associated with tuberculous infection and tuberculosis disease. Active smoking is significantly associated with recurrent tuberculosis and tuberculosis mortality. These effects appear to be independent of the effects of alcohol use, socioeconomic status and a large number of other potential confounders(15)

The cross-sectional study by Salami et al in Nigeria compares noncompliant pulmonary TB Patients (case group) with compliant patients (control group) on lifestyle and other factors as taken from medical records of treated smear positive patients. Noncompliance was an important issue in this sample population: over a nine year period, patients had a very high default rate of 44.2 %(769/1741) and 11.6% (202/1747) of the treated patients died. A significant odds ratio of 1.6 (95%CI=1.31-1.98; $p<0.001$) for default was found for cigarette smoking, without controlling for alcohol, but a final backward regression model did not include smoking. The authors expressed their belief that social demands/needs of patients might have led them back into smoking and drinking before completing their treatment. However, the study does not make clear whether the patients had stopped smoking or alcohol drinking during any part of their treatment. (16)

Despite the chronic nature of the illness, patients often presented with advanced disease resulting in high death rates during the first week of hospitalization. In a South African study while the mean time to death for all the case patients was 75 days, half the patients died within the first 19 days of admission. Thirty-two percent of the case patients died within the first week of hospitalization. Controls were hospitalized for a mean of 139 days (range, 6-474 days) (17)

Studies in some parts of Ethiopia- Southern region and Gondar area reported 74.8% and 29.5% treatment success rates in TB patients, respectively. These and various other studies in Southern region, Arsi zone, Gondar area, as well as Addis Ababa area of Ethiopia have documented independent risk factors for poor treatment outcome. These factors include attending the regional capital health centre, being on retreatment, having a positive smear at the second month follow-up, age being more than 55 years, being male, medication side effects, low body weight at initiation of anti-TB treatment (<**35** kg), year of enrollment, distance from home to treatment centre and the added burden of using public transport to get to a treatment centre (18, 19, 20)

Certain medical conditions were independently associated with death during treatment. Russian study at Orel showed cancer (adjusted odds ratio [AOR] 7.2), congestive heart failure (AOR 5.4), and chronic lung disease (AOR 2.4) as independent factors while diabetes and past history of tuberculosis were not significantly associated. In other study renal disease was significantly associated with increased mortality. In a large clinical trial in North America Cox multivariate regression analysis identified four independent risk factors for death after controlling for age: malignancy (hazard ratio [HR] 5.28, P <0.0001), HIV (HR 3.89, P <0.0001), daily alcohol (HR 2.94, P <0.0001), and being unemployed (HR 1.99, P <0.01). The risk of death increased with the number of independent risk factors present (P <0.0001). Extent of disease and treatment failure/relapse were not associated with an increased risk of death (4, 5, 11)

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Conceptual framework

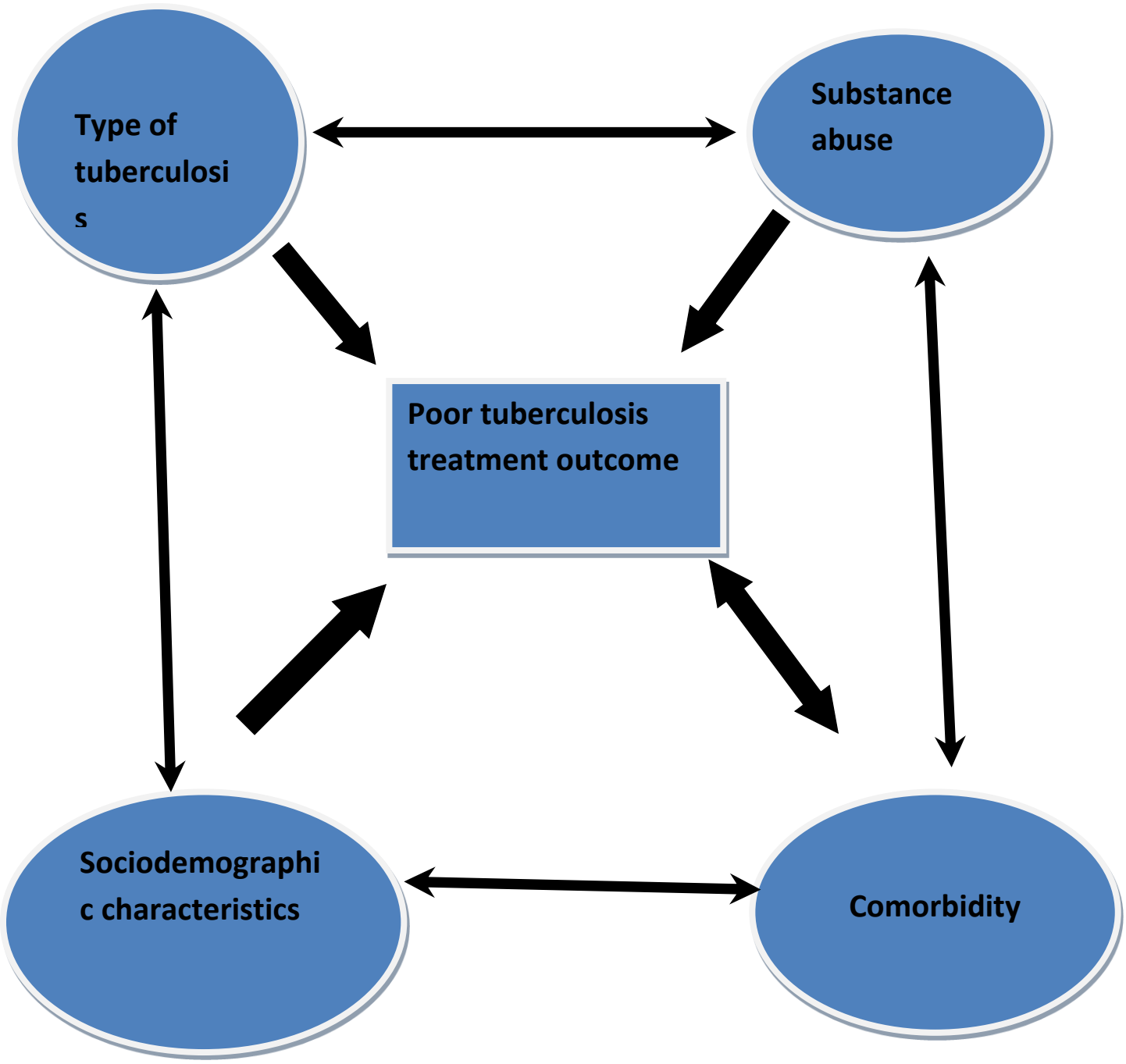

Figure 1 – conceptual framework of association between poor tuberculosis treatment outcome and variables

2.1 Significance of the study

Ethiopia is one of the 22 high burden countries and among the few who failed to show the needed progress to achieve the 50% mortality reduction in 2015.In this regard the need for detecting any possible modifiable factor that is responsible for unsuccessful outcome is of paramount importance. This work will serve to show treatment success rate, and effect of sociodemographic factors, substance abuse, co morbidity and type of tuberculosis on treatment outcome. It will identify patients with high risk of unsuccessful treatment outcome. This will serve as a baseline for interventional studies that aim improving tuberculosis treatment outcome.

Chapter 3. Objective

3.1 General objective

The objective of the study is to asses factors related to poor tuberculosis treatment outcome at JUSH between November 2013 and April 2014.

3.2 Specific objectives

- To describe basic characteristic of patients with tuberculosis.
- To identify socio-demographic factors associated with poor tuberculosis treatment outcome.
- To asses effect of co morbidity treatment outcome of patients with tuberculosis.
- To asses effect of type of TB on treatment outcome of patients with tuberculosis.
- To asses effect of substance abuse on treatment outcome of patients with tuberculosis.

4. Methods and materials

4.1 Study area:

The study was conducted in Jimma University specialized hospital, which is referral teaching hospital in the largest region of the country, Oromia regional state. Jimma University Specialized Hospital (JUSH) is one of teaching hospitals in the country with innovative curriculum of community based education. JU runs both undergraduate and graduate programs in several disciplines. The hospital gives health service at inpatient and outpatient level as a referral Hospital for 15 million populations in the South West of the country. Internal medicine department has five wards, 8 specialty clinics and cold and emergency outpatient departments. There were 267 tuberculosis patients inrolled in for treatment at Tb/HIV clinic last year.

4.2 Study period:

The study was conducted from November1, 2013 to April 2014.

4.3 Study design

Prospective cohort study was performed. There was no interventions related to the study, and all patients received the routine care following the hospital's guidelines.

4.4 Population

4.4.1 Source population

All patients visiting JUSH during the study period.

4.4.2 Study population

All adult tuberculosis patients who visited JUSH during the study period.

4.5 Inclusion and Exclusion Criteria

4.5.1 Inclusion criteria

Patients with active tuberculosis for whom physician decided to treat with a full course of tuberculosis chemotherapy were included.

4.5.2 Exclusion criteria

Age less than fourteen years and patients who refused to give consent were not included in the study

4.6 Sample size and Sampling procedure

All adult tuberculosis patients who were enrolled in the TB/HIV care unit of JUSH for the treatment of tuberculosis during the study period were included in the study. Patients who were referred to health centers in the catchment area of the hospital were followed with the existing link

4.7 Data collection and measurement

4.7.1Variables

4.7.1.1Dependent

Treatment outcome: successful (Cure and treatment completion) and poor (default, treatment failure and death)

4.7.2 Independent variable

- Age
- Sex
- Duration of symptom
- Substance abuse
- Living condition (urban, rural, prison, homeless, lonely, with a family)
- Co morbidity(anemia, HIV)

- Type of tuberculosis(based on Anatomic distribution, smear result, previous treatment history)

4.7.2 Operational definition

- **Tuberculosis** – physician decided to treat with full course of anti-tuberculosis chemotherapy.
- **Tuberculosis treatment success**-A patient whose treatment outcome is cure or who completed treatment.
- **Poor tuberculosis treatment outcome –** all tuberculosis treatment outcomes other than Cure and treatment completed
- **Alcohol abuse** – anyone who feels to stop drinking alcohol, who feels guilty about his drinking habit, who is annoyed by peoples comment on his drinking habit or anyone who uses alcohol as an eye opener.
- **Adult** – all patients above age of fourteen(since all individuals of age more than 14 get care in an adult unit in JUSH)

4.7.3 Data collection process and instrument

A structured questionnaire was prepared. Data was collected by a trained data collector. Questionnaires were filled at presentation, two months and six months. The questionnaires have three parts that assess socio-demographic characteristics, substance use pattern and clinical characteristics. The prepared questionnaires were pre-tested earlier on patients who were not part of the study before it is administered to the actual study group. Outcome of transferred patients to health centers in the catchment area were assessed using phone call on treatment completion through the existing link with the respective health centers and the TB/HIV clinic of JUSH. The completeness and relevance of the data collected was supervised by the principal investigator.

4.8 Data Analysis

The data was cleaned, edited and entered to SPSS window version 16 for analysis. Results were expressed as median ± SD or as percentages. The strength of correlation between the dependent and predictor variables are tested by using logistic regression analysis. A p-value of< 0.05 was considered as statistically significant.

4.9 Ethical Considerations

This study did not involve any potentially harmful intervention to the patient.Before official commencement of the data collection process, ethical clearance was obtained from the ethical committee of Jimma University. Every participant in the study was asked for his/her willingness to be involved in the study and written consent was obtained based on free will. The information collected from participants remained confidential. Names & other identifications of patients were not collected

4.10 Communication of Results

The results of this study will be submitted to the department of Internal Medicine, Jimma University and publishing it on scientific journals will also be considered.

Chapter 5. Results

5.1 Socio-demographic Characteristics

A total of 193 patients have visited adult tuberculosis follow up unit of Jimma university hospital during the study period; November 1, 2013 to April 2014. The response rate was 100%. There are 101(52.3%) males and 92(47.7%) female tuberculosis patients in the study. Age distribution of the study participants revealed that majority?(81.3%) are younger than 45 years. Students and farmers accounted for the majority, 55(28.5%) and 36(18.7%), respectively. Those unemployed accounted for 8.8% of the study subjects while fewer than five percent of the study populations were government employee. Only a single lady was a widow while four others reported divorce. Proportions of married and single individuals were similar. More than half of the study populations were Muslims (50.3%). Hundred twenty nine (66.8%) of patients live with their family while. Most of the patients (73.06%) have to use some form of transport to collect their medicine (see table 1).

Table1: Binary logistic regression of demographic characteristics of patients registered for TB treatment, JUSH.

Characteristics		Total No (%)	Outcome of treatment*		Crude OR	P-value
			Successful (0) No (%)	Poor(1) No (%)		
Sex	Male	101(47.7)	92(91.1)	9(8.9)	1.68	.26
	Female	92(52.3)	79(85.9)	13(14.1)	1	
Age(median ± SD)		26 ± 12.6	26	35	1.02	.14
Age in category	15-24	72(37.3)	71(98.6)	1(1.4)	0.16	
	24-35	60(31.1)	52(86.7)	8(13.3)	1.69	
	35-44	25(13)	15(60)	10(40)	7.33	
	≥45	36(18.7)	33(91.7)	3(8.3)	1	
Marital status	Married	96(50)	80(83.7)	16(16.7)	2.86	.22
	Single	91(47.4)	85(93.4)	6(6.6)	1	
	Divorced	4(2.4)	4(100)	0(0)	0.00	
	Widowed	1(.5)	1(100)	0(0)	0.00	
Ethnicity	Oromo	119(61.7)	108(91.8)	11(9.2)	0.55	.55
	Amhara	36(18.7%)	30(83.3)	6(16.7)	1.17	
	Tigre	6(3.1%)	6	-	-	
	Others	32(16.6%)	27(84.4)	5(5.6)	1	
Occupation	Student	55(28.5)	52(94.5)	3(5.5)	0.692	.13
	Farmer	36(18.7)	34(94.4)	2(5.6)	0.706	
	Government employ	9(4.7)	8(88.9)	1(10.1)	1.50	
	Private business owner	30(16)	23(76.7)	7(23.3)	3.65	
	House wife	33(17.6)	26(78.8)	7(21.2)	3.21	
	Unemployed	15(8)	14(93.3)	1(6.7)	.75	
	Others	11(5.9)	11(100)	-	1	
Religion	Muslim	97(50.3)	90(92.8)	7(7.2)	.253	.21
	Orthodox	74(38.3)	64(86.5)	10(13.5)	.508	
	Protestant	17(8.8%)	13(76.5)	4(23.5)	1	
	Catholic	5(2.6%)	4(80)	1(20)	.812	
Educational status	Cannot read and write	33(19.3%)	33(100)	-	-	.23
	Read and write	11(5.7)	8(4.7)	3(13.6)	16.87	
	Grade 1-7	52(26.9)	43(82.7)	9(17.3)	9.42	
	Grade 8-12	51(26.4)	42(82.4)	9(17.6)	9.64	
	Above 12	46(23.8)	45(97.8)	1(2.2)	1	
residence	Urban	126(65.6)	110(87.3)	16(12.7)	1.78	.29
	Rural	66(34.4)	61(92.4)	5(7.6)	1	
Living condition	With a family	129(66.8)	111(86)	18(14)	1	.34
	Lonely	6(3.1)	5(83.3)	1(16.7)	1.23	
	In a prison	14(7.3)	13(92.9)	1(7.1)	.474	
	In a charity cump	4(2.1)	3(75)	1(25)	2.06	
	Others	40(20.7)	39(97.5)	1(2.5)	1.6	
Transport use	Yes	141	123	18	1.76	.33
	No	52	48	4	1	

Note : * the reference category in the interpretation of the dependent variable was successful outcome (as it coded to be 0) comparing to poor outcome.

5.2 Substance Abuse

Chat chewing was the commonest substance abuse, nearly 40% of the subjects reported chat chewing habits but majority use only occasionally. Daily chat chewers accounted for 31.1%. thirty two patients(16.6%) drinks alcohol. Majority of patients who drink alcohol fulfill criteria for alcohol abuse (17(53.1%)). Twelve patients smoke cigarette. See table 2.

Table 2: Binary logistic regression of substance use and outcome of treatment among patients with tuberculosis in JUSH

Substance use			**Total No (%)**	**Outcome of treatment***		**Crude OR**	**P-value**
				Successful No (%)	**Poor No (%)**		
smoking	Yes		12(6.2)	12(100)	-	.00	.999
	No		181(93.8)	159(87.8)	22(12.2)	1	
Alcohol drinking	yes	No abuse	17(53.1)	15(88.2)	2(11.8)	1.57	.413
		Abuse	15(46.9)	12(80)	3(20)		
		Total	32(16.6)	27(84.4)	5(15.6)		
	No		161(83.4)	144(89.4)	17(10.6)	1	
Chat chewing	yes	Daily	23(31.1)	23(100)	-	.40	.09
		Weekly	14(18.9)	13(92.9)	1(7.1)		
		Occasionally	37(50)	34(91.9)	3(8.1)		
		Total	77(39.9)	72(93.5)	5(6.5)		
	No		116(60.1)	99(85.3)	17(14.7)	1	

Note : * the reference category in the interpretation of the dependent variable was successful outcome (as it coded to be 0) comparing to poor outcome.

5.3 Type of tuberculosis

One hundred twenty two patients were treated for tuberculosis of the lung with or without dissemination to other organ system and in a 72 patients tuberculosis was confined to extrapulmonary sites. Half(54.9%) of the patients with pulmonary involvement have a negative sputum smear examination for acid fast bacilli. Forty patients have disseminated tuberculosis. Lymph node, pleura and meninges were the most common extrapulmonary site involved in a descending order. Genitourinary tract involvement is reported in only three patients. See table 3.

Table 3: Binary logistic regression of type of tuberculosis and site of involvement among patients with tuberculosis in JUSH

type of tuberculosis			Total	Outcome of treatment*		Crude OR	P-value
				Successful no (%)	Poor no (%)		
Type of tuberculosis	Ptb	Smear +ve	40(32.8)	38(95)	2(5)	1	.259
		Smear –ve	67(54.9)	58(86.6)	9(13.4)	2.95	
		Smear not done	15(12.3)	12(80)	3(20)	4.75	
		total	122(63.2)	108(88.5)	14(11.5)	1.02	.97
	Extrapulmonary tb		71(36.8)	63(88.7)	8(11.3)	1	
Site of involvement	Lung		122(63.2)	108(88.5)	14(11.5)	0.98	.96
	pleura		24(12.4)	21(87.5)	3(12.5)	1.13	.86
	Lymph node		33(17.1)	31(93.9)	2(6.1)	4.52	.30
	Bone		13(6.7)	13(100)	0(0)	-	-
	pericardium		3(1.6)	3(100)	0(0)	-	-
	adrenal		15(7.8)	14(93.3)	1(6.7)	0.53	.55
	meninges		18(9.3)	12(66.7)	6(33.3)	4.97	.05
	GUT		3(1.6)	2(66.7)	1(33.3)	4.02	.26
	GIT		4(2.1)	4(0)	0(0)	-	-
	others		3(1.6)	2(66.7)	1(33.3)	4.03	.26

Note : * the reference category in the interpretation of the dependent variable was successful outcome (as it coded to be 0) comparing to poor outcome.

5.4 Co-morbidities and clinical variables of tuberculosis patients

Twenty percent of patients are HIV positive and 36% of patients are anemic. Half of the patients were admitted to hospital (49.2%) with a minimum in hospital stay of one day and maximum 126days. The median duration of hospital stay was 20± 2days. The minimum duration of illness is seven days while the median is 60 days. Tachypnea and tachycardia were the frequent unstable vital signs. Nine percent of patients reported previous tuberculosis treatment. See table 4.

Table 4: Binary logistic regression of co-morbidities and clinical variables of patients with tuberculosis at JUSH

Comorbidities and clinical variables		Total	Outcome of treatment*		Crude OR	P-value
			Successful no(%)	Poor no(%)		
HIV	**+ve**	40(20.7)	23(57.5)	17(42.5)	21.88	.001
	-ve	153(79.3)	148(96.7)	5(3.3)	1	
Hospitalization		94(49.2)	77(81.9)	17(18.1)	2.46	.08
Duration of illness	**<2wk**	2(1.3)	2(100)	-	-	.14
	2-4wk	25(14.5)	18(72)	7(28)	1	
	4-8wk	32(18.6)	30(93.8)	2(6.2)	.17	
	8wk-3mo	54(31.4)	49(90.7)	5(9.3)	.26	
	>3mo	59(34.3)	53(89.8)	6(10.2)	.29	
Previous Tb		17(8.8)	15(88.2)	2(11.8)	1.04	.96
Unstable Vital sign	**Tachypnea**	111(58.1)	95(85.6)	16(14.4)	.48	.15
	Fever	32(17.1)	28(87.5)	4(12.5)	1.00	.96
	Hypothermia	8(4.3)	7(87.5)	1(12.5)	1	
	Tachycardia	92(48.2)	79(85.9)	13(14.1)	.61	.28
	hypotenssion	9(4.8)	7(77.8)	2(12.2)	1.42	.57
	Hypertension	6(3.2)	5(83.5)	1(16.5)	1	
Anemia	**Yes**	51(36.2)	47(92.2)	4(7.8)	1	.25
	No	90(63.1)	87(96.7)	3(3.3)	.41	
Weight (mean + S.D)	**at initiation**	49.4 ± 9.4	49.6 ±9.6	47.4 ± 6.8	.97	.28
	at the end of 2 month	51.5± 9.4	51.4±9.4	52.4± 8.7	1.01	.81
	at the end of treatment	53.2 ±9.0	53.2±9.2	55 ± 1.2	1.01	.83

Note : * the reference category in the interpretation of the dependent variable was successful outcome (as it coded to be 0) comparing to poor outcome.

While patients have achieved sequencial weight gain as measured at initiation, end of intensive phase and end of treatment their was no statistically significant association with treatment outcome (p-value0.28, 0.81, and 0.83 respectively). See figure 1.

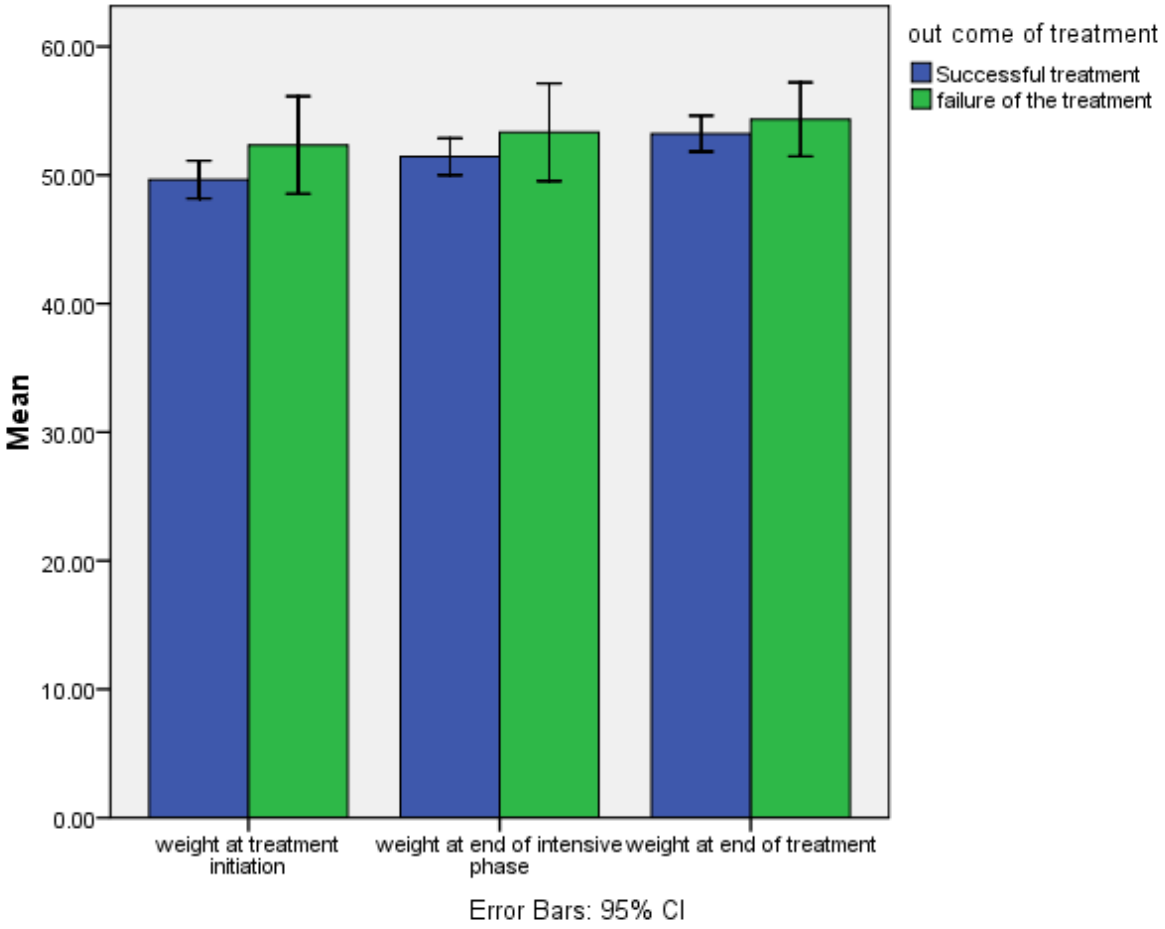

Figure 2 weight during follow up of tuberculosis patients on treatment and outcome at JUSH

The overall rate of poor tuberculosis treatment outcome is 11.5%. Major reason in the 22 patients with poor treatment outcome was death, taking twelve lives. Thirty three patient have got a cure from a smear positive pulmonary tuberculosis. Seventy one percent have completed treatment making the success rate 88.5%.

5.5 Multiple Logistic regressions of independent variables associated with poor tuberculosis treatment outcome

Though it is not statistically significant male sex confers 1.68 times higher poor tuberculosis treatment outcome than female sex. There is no statistically significant association between poor tuberculosis treatment outcome and sociodemographic factors like marital status, level of education, religion and occupation. Patients who reported that they chew chat have 60% less likelihoods of having poor tuberculosis treatment outcome (p-0.09). Alcohol drinking and smoking are not associated with poor treatment outcome.

Smear positive patients are more likely to have successful treatment outcome than smear negative though not statistically significant(p-0.26)

Meningeal involvement has a five times increased risk of poor outcome (4.97 p-value 0.05) Other sites of extra pulmonary involvement are not significantly associated with poor tuberculosis treatment outcome.

The only variable identified as independent risk factor for poor tuberculosis treatment outcome in this study is HIV status. HIV increases the risk of poor treatment outcome by 14.26(2.56 – 79.57) times (p-0.02). All dead patients were HIV positive. From the 22 patients with poor treatment outcome 17(77.27%) were HIV positive. Hospitalization increases the risk of poor tuberculosis treatment outcome 2.46 times though not statistically significant (p-0.08). The absence of anemia reduces the risk of poor treatment outcome by 60% but it was not statistically significant.

Table 5: Backward multiple logistic regression of HIV status with outcome of tuberculosis treatment at JUSH

Factor	**Total**	**Outcome of treatment***		**AOR (95% CI)**	**P-value**
		Successful no(%)	**Poor no(%)**		
HIV +ve	40(20.7)	23(57.5)	17(42.5)	14.26(2.56-79.57)	.002

Chapter 6. Discussion

Assessing treatment outcome of tuberculosis patients is of paramount importance. It is also clear that some factors can alter the outcome of tuberculosis treatment in a favorable or unfavorable manner. In this prospective health facility based study patients with pulmonary and extrapulmonary tuberculosis were followed during their treatment course to identify sociodemographic, substance use and clinical variables with an adverse impact on treatment outcome.

The sociodemographic characters of the population studied has a more or less similar picture with previous studies done in the same region on similar patient population by Ayalew and Halima. This is also true with other studies done in different parts of Ethiopia. This is an expected finding as the study period, study population geographic location socioeconomic and cultural profiles are similar for all Ethiopians (18, 17, 23, 3).

Though multiple retrospective studies documented significant association of unsuccessful treatment outcome with male sex, older age and unemployment in North Ethiopia(>40 years of age (adj. OR = 2.50, 95% CI: 1.12-5.59), unemployed (adj. OR = 3.10, 95% CI: 1.33-7.24) South Ethiopia(age >55 years (aOR 1.44, 95%CI 1.12–1.86) and being male (aOR 1.24, 95%CI 1.09–1.42)) and Gonder , in this study there was no statistically significant association with this variables and poor outcome. Possible rational explanation is the small size of the population studied which have a high success rate that didn't allow sufficient enough number of cases with poor treatment outcome to show the desired effect.(18, 17, 19)

Although there is a 60% non statistically significant reduction(COR-0.09) in poor tuberculosis treatment outcome in those who chew chat, their appears no significant association between substance abuse and poor treatment outcome in this study. The favorable effect of chat is probably due to its effect on immune cells. A study in Morroco showed that substance abuse(alcohol,cigarette and elicit drug use) as an independent risk factor for default and so for poor outcome. Marlucia da Silva Garrido and his colleagues from Brazil described a very significant association between default (poor outcome) and alcoholism (aOR 1.51; $p<0.001$). The fact that alcohol abuse and smoking among the study participants was low might contribute to the different stand of this study. (26,9, 23)

The rate of extra-pulmonary tuberculosis(36.8%) is a relatively higher figure when compared with 28.3 in a north west Ethiopian study. These could be due to the fact that the study was done in a referral hospital where challenging extrapulmonary tuberculosis cases are to be referred for a diagnosis and management. In this study there was no statistically significant association between type and site of tuberculosis except for meningeal involvement. It increase the risk of poor treatment outcome as high as fivefold (COR 4.97 P-0.05). (9)

The 20.7% prevalence of HIV associated tuberculosis is higher than the national reported figure of 17% which can be the effect of the setting being a referral hospital.HIV increases the likelihoods of poor treatment outcome more than 20 times (0.001). In Tanzania a study depicted that HIV was associated with increased mortality(HR of 3.7, 95% CI 2.6–5.2). Similarly in Brazil and Spain Co-infection with HIV/AIDS showed a statistically significant risk for default, aOR 1.62 ($p<0.001$) and (OR 9.93) respectively. (3, 24, 23, 7)

The rate of unsuccessful treatment outcome, 11.4%, is well lower than the national overall poor treatment outcome rate 23% of the 2010 data this is a result of ongoing effort with high commitment from the government and the overall socioeconomic changes in the country. The major reason behind poor outcome is death accounting for 54.55%, is a very high figure compared with studies in Mizan(1.22%) . This may be a miss diagnosis since culture and other invasive diagnostic tests are not well applied. No single individual has a treatment failure similar to that of the study in Mizan which involved 2043 tuberculosis patients where no individual has treatment failure. (25)

Chapter 7. Conclusion and Recommendation

7.1 Conclusion

The prevalence of poor tuberculosis treatment outcome in JUSH TB/HIV care clinic is 11.4%, a relatively higher figure. Nearly equivalent proportion of male and female subjects with majority in the early adult age (15-45) are getting the care. Most of the patients though have pulmonary tuberculosis, the proportion of extrapulmonary tuberculosis and HIV co-infection is high. The prevalence of smoking and alcohol abuse is low while chat chewing is quite high. This study also showed that involvement of meninges and co-infection with HIV significantly increases the rate of poor tuberculosis treatment outcome.

HIV co-infected tuberculosis patients needs a huge attention and a special care as the outcome could be worse. It is also same for patients with menigeal involvement. There is a need to work out how outcome of HIV associated tuberculosis could be improved. The impact of chat chewing needs clarification with a wider study because in this study the trend is towards reduction in poor treatment outcome.

Patients with HIV associated tuberculosis and those with mengeal involvement require close follow up in the care of the individual patient. Besides that, ways to improve care and outcome of such patients have to be sorted out by researchers in the university hospital in particular and in this country in general. Settling the impact of chat chewing on tuberculosis treatment outcome needs a prospective cohort study.

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Annex – 1

JIMMA UNIVERSITY

COLLEGE OF PUBLIC HEALTH AND MEDICAL SCIENCES

DEPARTMENT OF INTERNAL MEDICINE

A RESEARCH QUESTIONNAIRE, 2013/14

Thank you for your participation! your contribution will be highly valued as getting information from patients who are on treatment is crucial on this study. As I you understand the objective of the study is to determine factors associated with poor tuberculosis treatment outcome. So the data will be used to sort out risk factor for poor tuberculosis treatment outcome.

Data collectors code no _____

Part 1: sociodemographic characteristics

1. Age_____years
2. Sex 1) Male 2)Female
3. Marital status 1. Single 2. Married 3. Widow 4.divorced
4. Ethnicity 1. Oromo 2.Amhara 3.Tigray 4. Others(specifiy) _____
5. Religion 1.Muslim 2. Orthodox 3. Catholic 4.Protestant 5. Others(specifiy) _____
6. Educational status 1. Cannot read and write 2. Write and read 3. Grade 1-7
   4. Grade 8-12 5. 12+
7. Occupation 1. Farmer 2.Govt employed 3.student 4. Unemployed 5. House wife
   6. Private business owner 7. Others (specify) _____
8. Residence 1. Urban 2. Rural

9. How do you live?
    a. With a family
    b. Lonely
    c. In a Prison
    d. In a charity camp
    e. Homeless and resides on street
    f. Others_____

10. Do you have to use public transport to come to hospital 1)yes 2)no

Part 2: Questions on pattern of substance use

11. Do you smoke cigarette? 1)yes 2)no

12. Amount of cigarette in pack years_____

13. Do you a drink alcohol? 1)yes 2)no

14. Have you been in any of this

    a. Have you ever felt you ought to *c*ut down on your drinking?
    b. Have people *A*nnoyed you by criticizing your drinking?
    c. Have you ever felt *G*uilty or bad about your drinking?
    d. Have you ever had a drink first thing in the morning to steady your nerves or get rid of a hangover (*E*yeopener)?

15. Do you chew khat? 1)yes 2)no

16. How often do you chew chat

    a. Daily
    b. Weekly
    c. Occasionally
    d. On holydays only

Part 3: Clinical characteristics

17. Duration of illness_____

18. Previous tuberculosis treatment 1)yes 2)no

19. Outcome of previous treatment

    a. Cure
    b. Completed
    c. Default
    d. Failure
    e. unknown

20. Patient condition on initial presentation

    a. Respiratory rate _____
    b. Pulse rate_____
    c. Blood pressure_____
    d. Temperature_____
    e. Glasgow coma scale_____

21. Type of tuberculosis

    a. Smear +ve
    b. Smear –ve
    c. Smear note done

22. What are the involved organs

    a. Lungs
    b. Pleura
    c. Lymphnode
    d. Pericardium
    e. Meninges
    f. Adrenal
    g. Liver
    h. Spleen
    i. Spine
    j. Other bones

23. Hospitalization during diagnosis or treatment 1)yes 2)no

24. If you were hospitalized ;how long did you stay in the hospital_____

25. HIV test result

A. Positive

B. Negative

C. Unknown

26. Is their any Co morbidity _____

27. Sputum smear for AFB

	At initiation	End of intensive phase(IP)	One month after end of IP	At five month or later
Smear +ve				
Smear -ve				
Smear not done				

28. Weight at treatment initiation, two month and 5month or later_____,_____and _____

29. Culture and sensitivity if available _____

30. Hospital stay in days if any _____

31. Hemoglobin/hematocrite at initiation and completion of treatment respectively__

32. Outcome of treatment

a. Cure

b. Treatment completed

c. Default

i. Reason _____

1. Died
    a. Date of death_____
2. Transferred out
    a. Date of death_____
3. Treatment interrupted
    a. When dose the patient stopped taking drug
4. Outcome unknown

d. Treatment failed

i. Evidence

1. MDR at any time
2. Smear positive at or after 5 month of treatment

33. Name and signature of the data collectors _____Date_____

Annex III

Informed Consent Form

Date …….

Good Morning / Afternoon.

I am…….. , a physician / Nurse working in JUSH. We are conducting a research on prevalence, factors associated with poor tuberculosis treatment outcome at Jimma University Specialized Hospital. If you are willing, we want to involve you in the study and all we do is ask you some health related questions. Your participation is entirely based on your willingness and your refusal doesn't affect the service you get from us in any way.

The informations obtained from the interview,the measurements and your examination results will be kept confidential and will be used for the stated objectives only.

If you are convinced about its relevance and have decided to participate in the study, please put your name and signature in the space provided below. If you have any question about the study,you can contact us through the address stated at the end.

Name of participant……

Signature of Participant ……

Name of the principal Investigator …….

Signature of the principal investigator…….

Address of principal investigator ……

Annex IV

Date November 2013

To Jimma University Ethical Review Committee.

Subject: Request for Ethical Clearance.

I am a final year medical resident preparing to conduct a research entitled Factors Related to poor outcome in Patients With Tuberculosis in sub-Saharan Africa; Jimma experience This is the first research of its kind to be conducted in this setup and I hope it will give a clue about the magnitude of the problem and will serve as an entry point for further related researches.

I hereby request the committee to revise the proposal and grant me an ethical clearance to proceed with the research process.

With regards

Dr BerhanuWorku (Principal Investigator)

Name and signature of advisors

LejaHamza(internist)

Tariku Dejene (Msc)