Factors associated with tuberculosis treatment completion by Gender during 2014 - 2016 in Kampala, Uganda: A retrospective descriptive study

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Abstract

Background

To date, limited number of studies have explored the effect of gender in treatment outcomes in Uganda. No data on disaggregated treatment outcomes and influential factors by gender has been comprehensive compiled by the existing studies.

Objective

To determine the gender differences in TB patients treatment outcomes between 2014 and 2016 in Kampala in order to inform national policy and provide targeted interventions.

Methods

A retrospective cohort study using routine data of all eligible individuals who were initiated on first-line TB therapy between 2014 and 2016. De-identified data was obtained from all the Kampala divisions electronic TB registers, cleaned and analysed using STATA version 13.

Results

Of the 18,855 patients started on treatment during the study period, only 17,461 were included in the final analysis. Males were more likely to be 35 years or older, received DOT at facility yet females were more likely to be new patients. In addition, males were more likely to be pulmonary bacteriologically confirmed than females (OR 1.08 95% CI 1.00 - 1.17). Successful treatment completion and ART uptake were similar by gender. Of all outcomes, 83% were treatment successfully, 11% died, 1% treatment failed treatment and 5% got lost to follow-up. Compared to females, males were more likely to be lost from TB care and die compared to females.

Conclusion

Among TB patients in Kampala from 2014 to 2016, we found evidence that successful treatment completion is not influenced by gender. However other factors that may be associated with successful TB treatment completion include age, disease classification, HIV status and type of patient.

Background

Tuberculosis (TB) is an airborne-transmitted infectious disease with high morbidity and mortality around the world. According to the 2017 global TB report, an estimated 10.4 million people fell ill with TB in the previous year (Global TB report 2017). TB burden is more pronounced in African countries probably due to high HIV prevalence and so the continent accounts for about 25% of TB cases (Global TB report, 2017). In the above report, approximately 1.9 times males aged 15 years and old were diagnosed with TB worldwide compared to females in 2016.

While previous studies have reported gender disparities in health seeking behavior and treatment outcomes (Chandrashekhar T Sreeramareddy et al, 2014), late access to TB treatment and adherence coupled with health system challenges often lead to poor treatment outcomes and high mortality as well (Abhijit Mukherjee et al, 2012). Differences in health literacy, sociocultural factors, provider or system-level barriers, low degree TB suspicion index by health provider, the number and types of providers seen before TB diagnosis have been reported as contributing to the differences in TB clinical status at presentation, notification rates and TB treatment outcomes by gender (Dodor et al, 2005). These factors can be summarized into three broad themes: TB-related knowledge, education gender roles and status in the family. Surprisingly, despite facing more socioeconomic and cultural adversities women are less likely to die, fail or default from TB treatment compared to men (Jimenez-Corona ME et al, 2006).

To date, a limited number of investigators have explored the factors associated with treatment completion by gender especially within a single cohort in Uganda. In addition, most studies of gender and TB have been conducted in high resource settings, and the extent to which differences in management by gender persist in low-resource contexts is not clear.

Uganda ranked among world's 30 countries with a high TB/HIV burden, has the TB prevalence of about 253 per 100,000 population and the average ratio of male to female in bacteriologically confirmed TB cases as 4.0 (Uganda TB prevalence survey, 2015). The country has an annual average TB treatment success rate of 75% while Kampala's has been about 68% which is below the 85% target.

Factors associated with loss to follow up from anti-TB treatment are old age (De Albuquerque et al. 2007), being male, and low education level (Tissera 2003). Migration for work, perception that TB is incurable and poor knowledge about TB also increase the risk for loss to follow up (Vijay et al. 2003), as do low income and poor attitude of heath care workers (Dodor & Afenyadu 2005; Holtz et al. 2006). Thus knowledge of patient factors associated with unfavourable treatment outcomes is crucial in developing strategies to improve treatment success rates. We investigated factors associated with treatment completion by gender in Kampala, Uganda.

Methods

Study design

This was a retrospective study of bacteriologically or clinically proven TB patients started on anti-TB treatment in 63 health facilities in Kampala in Uganda, January 2014 to December 2016. The 63 health facilities included 2 national referral hospitals, 2 regional referral hospitals, 15 general hospitals, 7 health centre IVs, 23 health centre IIIs, 4 health centre IIs and 10 clinics.

Settings

General settings

Kampala is Uganda's capital city with a population of 1,583,000 people and 91% of the population stay in urban setting. TB control is supervised by the National TB and Leprosy control Program (NTLP) under Ministry of Health. TB diagnosis and treatment services are integrated into the general health care.

TB diagnosis was based on clinical examination, sputum smear microscopy, chest radiography, GeneXpert®, and other investigations as appropriate for extra-pulmonary disease. Providers documented patient's demographic and clinical information in a unit TB registers at treatment initiation and drug dispensing information during treatment follow-up. TB patients were initiated on treatment on in-and outpatient's basis. Treatment consisted of a 2-month intensive phase of Rifampicin, Isoniazid, Pyrazinamide and Ethambutol followed by a 4-month continuation phase of Rifampicin and Isoniazid. Patients were scheduled to pick-up TB drugs at bi-weekly in intensive and monthly in continuation phases respectively. Upon completion of the treatment and the necessary follow up investigation, treatment outcomes were assigned according to the WHO's definition. Certificates were given to patients who successfully completed the treatment.

Study population

All TB patients diagnosed between January 2014 to December 2016 in Kampala were included in the study. However patients diagnosed and initiated on treatment from outside Kampala excluded because it was difficult to gather their complete records. Also non-transferred out patients whose final treatment outcomes could not established were excluded from the study as health workers did not know what happened to them.

Data management and Analysis

Data was extracted from TB electronic registers of 63 health facilities into STATA version 13. Independent variables were chosen from the registers based on plausibility and previous evidence of association from the literature. Data was checked for consistency, completeness, clarity and accuracy before analysis.

Descriptive statistics included calculating the mean, median and mean age, and proportions of different patient characteristics. Comparative bivariate tests Pearson's chi-square and two sample t-test was used for categorical variables to evaluate associations between dependent and independent variables. All variables with a p-value less or equal to 0.20 at the bi-variable analysis stage were included in a logistic regression to identify factors associated with treatment completion by gender.

In addition, collinearity and confounding elements among factors were checked and removed from the final model. The association was considered significant between predictor variables with the dependent variable if the p-value was < 0.05. Odds ratios and their corresponding 95% confidence interval (CI) were reported as the measures of association.

Ethical considerations

Prior to data collection, ethical approval was obtained from the School of Medicine Research and Ethics Committee – Makerere University College of Health Sciences and Uganda National Council of Science and Technology. No patient identifier information was collected as a way of maintaining confidentiality.

Aim Of The Study

To explore factors associated with treatment completion among TB patients initiated on first line TB therapy between 2014 and 2016 in Kampala city (Uganda). The study will inform national policy and provide targeted gender based interventions aimed at reducing disproportionate TB burden in the country.

Specific Objectives

1. To calculate proportions of TB patients who successfully completed treatment by gender of TB patients initiated on first-line TB therapy during 2014- 2016 in 63 health facilities in Kampala.
2. To assess gender related factors affecting TB treatment completion of patients initiated on first line TB therapy during 2014- 2016 in 63 health facilities in Kampala.

Results

Between 2014 and 2016, 18,855 TB patients were registered for treatment in the 63 health facilities in Kampala. A total of 1394 patients were excluded from the study; because 1,111 (6%) started treatment at facilities outside Kampala and 283 (2%) had no treatment outcomes. The remaining 17,461 were included in the study for analysis. Of these, 10,877 (62%) were males. The median age at treatment registration was 30 years (interquartile range (IQR) 24 - 40) with 35% of the patients aged 35 years and above.

While patients were proportionately distributed by level of care and gender, about 65% of the patients were treated from government owned health facilities. While the rest of patients were distributed in the facilities located in the 5 administrative divisions of Kampala, 39.1% were treated from Mulago which is the national referral hospital for the country.

Table 1 shows distribution of baseline characteristics by gender. Males were more likely to be 35 years or older, received DOT at facility yet females were more likely to be new patients. In addition, males were more likely to be pulmonary bacteriologically confirmed than females (OR 1.08 95% CI 1.00 - 1.17).

All patients were tested for HIV, 48.9% of them were found to be TB/HIV co-infected and 92.7% of those co-infected were initiated on ART at the beginning of TB treatment. However males were less likely to be diagnosed HIV positive and being new TB patients at diagnosis than females (HIV positive: OR 0.70 95% CI 0.65 - 0.74; New TB patients: OR 0.58 95% CI 0.49-0.68).

Successful treatment completion and ART uptake were similar by gender. Of all outcomes, 83% were treatment successfully, 11% died, 1% treatment failed treatment and 5% got lost to follow-up. Compared to females, males were more likely to be lost from TB care and die compared to females ($p<0.001$).

A logistic regression model (see table 2) showed that clinically and extra-pulmonary diagnosed patients were likely to successfully complete treatment compared to bacteriologically confirmed patients for both males and females. Across both gender, new patients were more likely to successfully complete treatment compared to their previously treated patients. Also between both males and females, having negative HIV status was significantly associated with successful treatment completion compared to having positive HIV status.

On the other hand, young age among males was found to be significantly associated successful treatment completion compared to female counterparts. Compared to males aged between 0 – 14 years old, age categories between 5 – 14 years (Adj. OR 2.02 95% CI 1.26 – 3.24), 15 – 24 years (Adj. OR 1.91 95% CI 1.34 – 2.71) and 25 – 34 years (Adj. OR 1.39 95% CI 1.00 - 1.94) supported above finding.

Patients treated from general hospitals, health centres IVs and IIIs were significantly more likely to successfully complete treatment across gender compared their counterparts treated from the 2 national referral hospitals. Furthermore, female patients treated from private clinics had a higher odds (Adj. OR 2.04 95% CI 1.04 - 4.01) of compared to their counterparts at the national referral hospitals.

Discussion

Among TB patients in Kampala from 2014 to 2016, we found evidence that successful treatment completion is not influenced by gender. Although impact of gender on treatment outcomes of TB patients has been evaluated in previous studies, has revealed inconsistent results. This finding is consistent with studies carried out in Brazil and Egypt (Kamel MI, et al 2003).

However in those with unfavorable treatment outcomes, more males got lost to follow up compared to females. The similarities observed in our setting were consistent with the international literature (J. –Y Yeng et al, 2012, K. Dale et al, 2015). Overall, these observations are consistent with the hypothesis that under normal circumstances, males and females have the same chance of successfully completing TB treatment in Kampala.

We found that while more females were TB/HIV co-infected and new on TB treatment, males were more likely to be pulmonary bacteriologically confirmed compared to counterparts. These findings are consistent with other studies carried out in cities and urban settings like Kampala (Abhijit Mukherjee, et al 2012). Strengthening health provider-initiated TB screening capacity using the NTLP recommended job aid may provide opportunity for early TB case finding and prompt treatment initiation

On the other hand, socioeconomic barriers may also exist and hinder healthcare-seeking behavior in women. Therefore under-diagnosis of TB in women is a pivotal issue in TB management and should be carefully evaluated in Uganda and other under developed countries. Regarding clinical presentations, females were found to be less symptomatic as compared with male patients just like in the Uganda prevalence survey report. Also a national tuberculosis survey in Bangladesh described a lower awareness of symptoms among female TB patients (Hamid Salim MA, 2004). The absence of respiratory and

constitutional symptoms may lead to a delay in seeking medical assistance. Less advanced radiographic findings also make it less likely that health workers will suspect pulmonary TB. Although details about delays in diagnosis were not collected in the present study, all of these factors may contribute to a delayed or low diagnosis of bacteriologically confirmed TB in women as suggested by this study.

Mortality in TB patients is mainly affected by age, disease classification, ART uptake and health facility level of care. This means that younger, clinically diagnosed or extra-pulmonary who are treated from lower levels of care are prone to death. Providing ART to TB/HIV co-infected immediately during TB treatment reduces the risk of dying or getting lost to follow up. These findings disclose the differences between male and female TB patients with regards to clinical characteristics and possible impact on treatment outcomes. We did not divide deaths as being TB related or non-TB related due to the difficulties in evaluating the impact of TB on mortality. All-cause mortality is more objective and applicable in clinical practice.

Conclusions

Furthermore the study was performed in an under developed country with a high HIV prevalence, and ART initiation may have not been prompt and routine among all TB/HIV co-infected patients. This may limit the ability of our findings to be applied to high to middle-income countries or low HIV endemic areas.

Since getting lost to follow up during TB treatment was influenced by male gender and patient type, instituting gender-specific strategies in TB management like getting family or community support for male patients could reduce unfavourable treatment outcomes. Integration of TB and HIV services especially for counselling may also allow for efficient delivery of important information to patients. Further studies focusing on immunological characteristics are also warranted to elucidate gender related factors other than socio-cultural and clinical factors.

There are several limitations to this study. The duration of presenting symptoms or extent of disease before diagnosis was not recorded in our patients, yet this may influence outcomes. Study hospitals included a national referral hospital where patients with a higher severity or co-morbidities may have been included.

We also acknowledge that interpretation of the strength of our findings should be considered in the context of multiple statistical comparisons, and that the potential for type-1 errors exists. The differences that we reported were generally small-to-moderate in magnitude, and caution should be taken in ascribing too much importance to any single finding.

Abbreviations

TB Tuberculosis

OR Odds Ratio

ART Antiretroviral Therapy

HIV Human Immunodeficiency Virus

NTLP National TB and Leprosy control Program

WHO World Health Organization

CI Confidence Interval

DOT Directly Observed Therapy

Declarations

Ethics approval and consent to participate:

Ethics approval was obtained from the Makerere University College of Health sciences research ethics review board. As secondary data were used, the need for informed patient consent was waived.

Consent for publication

Not applicable

Availability of data and material

The data collected and used for the study is available and there is no objection from Uganda Ministry of Health to share this data

Competing interests

Authors declare no competing interest

Funding

Not applicable

Authors' contributions

(EA, MPS, AB, FM, IK & HT are initials e.g. Hannock Tweya -> HT)

EA conceived the study; EA designed the study protocol; EA, MPS, AB, FM and HT implemented the study. EA and HT carried out analysis and interpretation of these data. EA and HT drafted the manuscript; MPS, AB, FM & IK critically revised the manuscript for intellectual content. All authors read and approved the final manuscript. EA and HT are guarantors of the paper.

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Tables

Table 1: Characteristics of TB patients treated from Kampala 2014 - 2016 (n = 17,461)

Variables	Sex					
	Total		Male		Female	
	Number	Percent	Number	Percent	Number	Percent
Age category (Years)						
0 - 4	497	2.8	270	2.5	227	3.4
5 - 14	525	3.0	265	2.4	260	3.9
15 - 24	3,538	20.3	1,890	17.4	1,648	25.0
25 - 34	6,125	35.1	3,766	34.6	2,359	35.8
35 - 44	3,991	22.9	2,771	25.5	1,220	18.5
45 - 54	1,880	10.8	1,312	12.1	568	8.6
55 - 64	586	3.4	405	3.7	181	2.7
65 +	319	1.8	198	1.8	121	1.8
Health division						
Mulago national referral Hospital	6832	39.1	4130	38.0	2702	41.0
Kawempe division	1951	11.2	1164	10.7	787	12.0
Rubaga division	2277	13.0	1405	12.9	872	13.2
Makindye division	2162	12.4	1339	12.3	823	12.5
Nakawa division	1572	9.0	1069	9.8	503	7.6
Central division	2667	15.3	1770	16.3	897	13.6
Health Facility Ownership						
Government	11297	64.7	7142	65.7	4155	63.1
Private Not For Profit	4829	27.7	2933	27.0	1896	28.8
Private For Profit	1335	7.6	802	7.4	533	8.1
Health Facility Level of Care						
National Referral Hospital	7053	40.4	4278	39.3	2775	42.1
Regional Referral Hospital	754	4.3	497	4.6	257	3.9
General Hospital	3177	18.2	1999	18.4	1178	17.9
Health Centre IV	1660	9.5	1134	10.4	526	8.0
Health Centre III	4323	24.8	2673	24.6	1650	25.1
Health Centre II	242	1.4	138	1.3	104	1.6
Clinic	252	1.4	158	1.5	94	1.4
Type of Tuberculosis						
Pulmonary Bacteriologically Confirmed	10418	59.7	6625	60.9	3793	57.6
Pulmonary Clinically diagnosed	4053	23.2	2520	23.2	1533	23.3
Extra-Pulmonary	2990	17.1	1732	15.9	1258	19.1
Type of TB patient						
New on TB treatment	16154	92.5	9926	91.3	6228	94.6
Return after relapse	885	5.1	633	5.8	252	3.8
Return after lost to follow up	314	1.8	249	2.3	65	1.0
Return after Failure	107	0.6	69	0.6	38	0.6
Treatment History Unknown	1	0.0	0	0.0	1	0.0

HIV Status						
Positive	8540	48.9	4951	45.5	3589	54.5
Negative	8921	51.1	5926	54.5	2995	45.5
ART given						
Yes	7919	92.7	4597	92.8	3322	92.6
No	621	7.3	354	7.2	267	7.4
DOT status						
Facility Based DOT	411	2.4	309	2.8	102	1.5
Community Based DOT	12448	71.3	7657	70.4	4791	72.8
Not Recorded	4602	26.4	2911	26.8	1691	25.7
Treatment outcomes						
Cured	7879	45.1	4947	45.5	2932	44.5
Treatment Completed	6611	37.9	4064	37.4	2547	38.7
Died	1867	10.7	1107	10.2	760	11.5
Failure	166	1.0	109	1.0	57	0.9
Lost to Follow Up	938	5.4	650	6.0	288	4.4

Table 2: A logistic regression of Treatment completion and patients factors by gender among TB patients, Kampala 2014 – 2016 (n = 17,461)

	Male gender				Female gender			
	Univariate		Multivariate		Univariate		Multivariate	
	OR (95% CI)	P-value	Adjusted OR (95% CI)	P-value	OR (95% CI)	P-value	Adjusted OR (95% CI)	P-value
Age category (Ref = 0 - 4 Years)								
5 - 14 Years	1.96 (1.23 - 3.13)	0.004	2.02 (1.26 - 3.24)	0.003	1.40 (0.83 - 2.36)	0.211	1.33 (0.78 - 2.28)	0.297
15 - 24 Years	2.34 (1.69 - 3.23)	<0.001	1.91 (1.34 - 2.71)	<0.001	1.27 (0.86 - 1.87)	0.230	1.34 (0.75 - 1.74)	0.545
25 - 34 Years	1.41 (1.04 - 1.90)	0.026	1.39 (1.00 - 1.94)	0.047	0.93 (0.63 - 1.35)	0.689	1.15 (0.76 - 1.73)	0.514
35 - 44 Years	1.23 (0.91 - 1.67)	0.181	1.32 (0.95 - 1.84)	0.102	0.78 (0.53 - 1.15)	0.210	1.07 (0.70 - 1.63)	0.758
45 - 54 Years	0.95 (0.70 - 1.31)	0.778	1.03 (0.73 - 1..46)	0.845	0.65 (0.43 - 0.97)	0.037	0.83 (0.53 - 1.29)	0.401
55 - 64 Years	1.05 (0.72 - 1.53)	0.004	1.06 (0.71 - 1.58)	0.758	0.49 (0.30 - 0.80)	0.004	0.56 (0.33 - 0.94)	0.029
65 + Years	0.76 (0.50 - 1.17)	0.219	0.69 (0.44 - 1.08)	0.107	0.37 (0.22 - 0.62)	<0.001	0.33 (0.19 - 0.58)	<0.001
Disease classification (Pulmonary Bacteriologically Confirmed)								
Pulmonary Clinically diagnosed	0.61 (0.55 - 0.69)	<0.001	0.67 (0.59 - 0.76)	<0.001	0.60 (0.52 - 0.71)	<0.001	0.67 (0.56 - 0.79)	<0.001
Extra-Pulmonary	0.54 (0.47 - 0.62)	<0.001	0.60 (0.53 - 0.69)	<0.001	0.46 (0.39 - 0.54)	<0.001	0.58 (0.49 - 0.69)	<0.001
Patient type (Previously treated)								
New patient	1.65 (1.29 - 2.13)	<0.001	1.58 (1.34 - 1.86)	<0.001	1.65 (1.29 - 2.13)	<0.001	1.65 (1.27 - 2.14)	<0.001
HIV status (HIV Positive)								
HIV Negative	1.86 (1.68 – 2.06)	<0.001	1.70 (1.52 – 1.90)	<0.001	2.61 (2.26 - 3.01)	<0.001	2.58 (2.20 – 3.02)	<0.001
Health Facility Level of Care (National referral Hospital)								
Regional Referral Hospital	1.22 (0.96 - 1.57)	0.107	1.15 (0.88 - 1.50)	0.314	1.65 (1.14 - 2.39)	0.007	1.38(0.93 - 2.06)	0.108
General Hospital	1.66 (1.43 - 1.93)	<0.001	1.71 (1.46- 2.00)	<0.001	1.95 (1.60 - 2.38)	<0.001	1.89 (1.53- 2.32)	<0.001
Health Centre IV	1.42 (1.19 - 1.70)	<0.001	1.26 (1.04 - 1.51)	0.015	1.99 (1.50 - 2.64)	<0.001	1.81 (1.35 - 2.42)	<0.001
Health Centre III	1.22 (1.08 - 1.39)	0.002	1.32 (1.15 -1.50)	<0.001	1.34 (1.14 - 1.57)	<0.001	1.52 (1.28 -1.80)	<0.001
Health Centre II	1.18 (0.76 - 1.85)	0.461	1.02 (0.65 - 1.61)	0.925	1.33 (0.79 - 2.26)	0.284	1.38 (0.80 - 2.38)	0.248
Clinic	1.46 (0.93 - 2.29)	0.097	1.33 (0.84 - 2.11)	0.216	2.19 (1.13 - 4.25)	0.020	2.04 (1.04 - 4.01)	0.039
Health Facility ownership (Government)								
Private not for profit	1.16 (1.03 - 1.30)	0.013			1.28 (1.10 - 1.48)	0.001		
Private for profit	1.50 (1.21 - 1.86)	<0.001			1.61 (1.22 - 2.11)	0.001		
Directly Observed Therapy (Facility DOT)								
Community Based DOT	0.90 (0.65 - 1.25)	0.542			1.26 (0.76 - 2.09)	0.364		

Annex 1: Operational Definition

According to the standard definitions adopted from WHO, the following clinical case and treatment outcome operational terms will be used:

Pulmonary Bacteriologically Confirmed TB patient (P-BC)

A patient with Genexpert sputum test results MTB detected or at least one sputum specimen which with positive for acid fast bacilli (AFB) by microscopy.

Pulmonary Clinically Diagnosed TB patient (P-CD)

A patient who does not fulfil the criteria for bacteriological confirmation but has been diagnosed with active TB by a clinician or other medical practitioner who has decided to give the patient a full course of TB treatment. This includes cases diagnosed on the basis of X-ray abnormalities or suggestive histology and Extra Pulmonary cases without laboratory confirmation.

Extra Pulmonary TB patient (EPTB)

This is a patient with TB in the organs other than the lungs, such as lymph nodes, abdomen, genitourinary tract, skin, joints and bones, the meninges and others.

According to WHO, treatment outcomes were categorized into, successful treatment completion is if TB patient cured (negative smear microscopy at the end of treatment and on at least one previous follow-up test) or completed treatment with resolution of symptoms.

Unsuccessful treatment completion on the other hand is if treatment resulted in treatment failure (remaining smear-positive after 5 months of treatment), getting lost to follow up (patients who interrupted their treatment for two consecutive months or more after registration), or died.