Effect of COVID-19 Period on Tuberculosis Treatment Success; a Mixed Methods Study among Tuberculosis patients at Jinja Regional Referral Hospital.

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Research Article

Keywords: Corona Virus Disease 2019, Directly Observed Treatment, Short-course, Tuberculosis, Pulmonary TB, Severe Acute Respiratory Syndrome, Multidrug-resistant tuberculosis

Posted Date: September 20th, 2022

DOI: https://doi.org/10.21203/rs.3.rs-2056991/v1

Abstract

Introduction

Before the COVID-19 pandemic, over 4000 people were dying from TB every day. TB is still a major public health threat globally, but the TB epidemic may be exacerbated by the COVID-19 pandemic. The lockdown in response to the pandemic and the events related to it can have an adverse epidemiologic impact on TB treatment outcome through its effect on poverty, and dietary intakes.

Objectives

Therefore, this study during COVID-19 would determine the effect of COVID-19 period on Tuberculosis Treatment success among TB patients.

Methods

Sequential explanatory mixed methods was used. A retrospective cohort study was employed for the quantitative component to determine the association between COVID-19 period and Tuberculosis treatment success among Tuberculosis Patients at Jinja Regional Referral Hospital. A data abstraction sheet was used to extract the required data from the TB treatment registers. Treatment outcomes was dichotomized as successful treatment outcome and poor treatment outcome. Modified possion regression was used to explore associations between treatment outcome and other independent variables.

A qualitative study with a phenomenology approach was adopted to get an in-depth understanding to the barriers and facilitators to treatment success during the COVID era among Tuberculosis Patients at Jinja Regional Referral Hospital. The lived experience of the TB patients who had participated in the quantitative component was captured. Data from audio recordings was transcribed and analyzed using a deductive thematic analysis to explore barriers and facilitators.

Results

There was no significant effect of COVID-19 Period on TB treatment Success (aRR=1.04: 95% CI 0.78-1.38). In addition, sex, HIV status, age, distance from the health facility, disease classification and treatment mode were not significantly associated with treatment success. The barrier to treatment success were lack of adequate health care information, fearing the COVID thing in the hospital. Some health workers pointed out that donors failed to support most of the TB activities as government redirected most of its funding to COVID-19 activities and neglected TB services.

The major facilitators were good relationship with health care workers, TB awareness programs, updating of TB guidelines and availability of free drugs and services.

Conclusion

This study did not find a significant effect of COVID-19 period on treatment outcomes. Measures towards alleviating fear and stigma and ensuring financial securities of the patients during the time of health crisis are important for preparedness against future epidemics such as COVID-19.

Background

An estimated 10 million people developed the TB with an estimated 1.2 million related Tuberculosis(TB) deaths in 2019 (1). Sub-Saharan Africa carries the biggest burden with 95% of global TB deaths(2). Uganda, like the rest of Sub-Saharan countries, is plagued by the dual TB and HIV epidemics and is the seventh in the 22 countries with the highest TB prevalence(1). TB is still a major public health threat globally, but the TB epidemic may be exacerbated by the COVID-19 pandemic.(3, 4). Reports have suggested that TB detection and health care declined during worldwide lockdowns(5, 6). Designated hospitals that previously served for TB diagnosis and treatment had been identified as designated hospitals for COVID-19 diagnosis and treatment including Jinja Regional Referral Hospital(7). Meanwhile, suspected and confirmed TB cases might have been reluctant to go to hospital for fear of COVID-19 infection. This might have caused diagnostic delays for the suspected TB patients but increase the risk of TB transmission in households and communities.

Globally the treatment success rate (TSR) for new cases is 85%, with Africa at 82% (1). In 2020, Angola had the lowest TB TSR of 34% and Burundi has the highest TSR of 92% in Africa(1). The TSR in East Africa was 72% in 2020 (1). This is substantially lower than WHO recommended treatment success of 90% which could be related to the limited evaluation of treatment outcomes in countries with limited resources and to the presence of factors that affect the outcome of TB treatment(8).

The annual health sector performance report for Uganda in financial year (FY) 2019/20 shows TB TSR increased by 6–78% from 72% in FY 2018/19(9). This was contributed to by a collaborative quality improvement effort which involved 45 focus facilities in improving adherence to treatment and TB preventive therapy. The Annual Health Sector Development Plan target of 90% was not achieved(9). TB treatment success rates were highest in the districts of Butebo (124%), Serere (98%), Kitgum (97%), Kyankwanzi (97%). Districts with the lowest TB TSR were; Jinja (47%), Nabilatuk (42%) and Mukono (30%)(9). These low TSR could increase transmission, remergence of drug resistance and relapse of patients(10).

The COVID-19 pandemic could be compared to the Ebola outbreak in Liberia in 2014, where case notifications declined and the TB treatment success rate dropped from 80–69%(11–13). The success rate increased during the post-Ebola period, but remained low at 77%, indicating the impact on TB treatment outcomes(13). Some of the reasons for this decrease included closure of the health facilities and laboratories, healthcare workers becoming sick, stock out of medical supplies and repurposing of existing facilities and staff (12). To contain the spread of COVID-19, most African countries implemented lockdowns with Uganda instituting a lockdown on 26th March 2020(14).

The lockdown in response to the COVID-19 pandemic and the events related to it could have an adverse epidemiologic impact on TB incidence through its effect on poverty and dietary intakes(15). Exhaustive estimates of TB treatment outcomes are needed to improve the programmatic management of TB since the COVID-19 pandemic threatens to reverse recent progress in reducing the global burden of TB disease. COVID-19 led to massive health system disruption with the cancellation of routine health services in many settings (16, 17).

Therefore, this study before and during COVID-19 would provide estimated levels of treatment outcomes and associated factors among TB patients.

Problem Statement

Uganda is one of the 22 high burden TB countries that collectively account for 90% of the global TB burden(1). Uganda like other high TB burden countries has failed to achieve both targets of 90% treatment coverage and 90% treatment success in 2020 Jinja district has a TB incidence rate of 292/100,000 which is above the Uganda national average of 201/100,000(18). TB is treatable but due to several challenges which are closely connected with social and economic conditions such as age, gender, rural residence, the type of TB, HIV status and lack of treatment these make its prevention, care, and control more challenging(19–21).

Many of the TB related morbidities are preventable by early diagnosis and appropriate treatment; however, owing to various reasons, its management is not always that easy (21). COVID-19 caused TB health service disruptions such as decreases in diagnostic activities and clinic visits, delays in diagnosis and treatment initiation, interruptions in drug supply and reduced treatment support(15). Its anticipated these disruptions had an effect on adherence leading to increased morbidity and drug resistance. Identifying its associated factors is an integral part of the treatment.

Therefore, designing effective strategies for reducing TB morbidity and mortality, improving TB treatment outcomes and ending the global TB epidemic hence the need to estimate the associated factors among TB patients most especially during double epidemic like for COVID-19 and TB and the barriers and facilitators to these treatment outcomes.

Justification

The Global plan to end TB 2018–2022 centered on the End TB strategy of the 90-(90)-90 targets for TB, providing an ambitious plan to drive bold action and determined change. The plan demands that all TB stakeholders such as governments, country programs, civil society, communities, technical partners, international organizations and private sector to work together to reach at least 90% of the people with TB including key and vulnerable populations, place them on appropriate treatment, and ensure that at least 90% of them have a successful completion(22, 23).

The national tuberculosis and leprosy program strategic plan 2016–2020, set a target for Uganda to reach a treatment success rate for the tuberculosis at 90%. But Uganda failed to reach this target in 2020.

Areas of Busoga region had a treatment success rate of 83% which is still below the national TB treatment success rate target. Busoga region has had a lot of improvement in TB services and it was hypothesed that it would hit the national TB treatment success target in 2020(24).

The COVID-19 pandemic resulted in both a health shock and an economic shock. The lockdown in response to the pandemic and the events related to it can have an adverse epidemiologic impact on TB incidence through its effect on poverty, dietary intakes and access to health care.(15). COVID-19 led to massive health system disruption with the cancellation of routine health services in many settings (16, 17). There is no study fully discussing the short-term effect of COVID-19 period on TB treatment outcomes with real data of country emerged from this crisis.

Therefore, this study will help to improve successful provision for frontline health during future pandemics by helping to revise the implementation of TB services and allocate resources to different TB interventions.

Research Question

1. Is there an association between COVID-19 period and Tuberculosis treatment success among Tuberculosis Patients at Jinja Regional Referral Hospital?
2. What are the facilitators and barriers to treatment success during the COVID era among Tuberculosis patients at Jinja Regional Referral Hospital?

Research Objectives

Main Objectives

To determine the Effect of COVID-19 on Tuberculosis Treatment success among Tuberculosis Patients at Jinja Regional Referral Hospital from March 2019 to May 2021.

Specific Objectives

1. To determine the association between COVID-19 period and Tuberculosis treatment success among Tuberculosis Patients at Jinja Regional Referral Hospital.
2. To explore the facilitators and barriers to treatment success during the COVID era among Tuberculosis Patients at Jinja Regional Referral Hospital.

Literature Review

Definitions

Tuberculosis (TB) is an infectious disease caused by the bacillus Mycobacterium tuberculosis. It typically affects the lungs (pulmonary TB) but can affect other sites as well (extra pulmonary TB). The disease is

spread in the air when people who are sick with pulmonary TB expel bacteria, for example by coughing. In general, a relatively small proportion of people infected with mycobacterium will go on to develop TB disease; however, the probability of developing TB is much higher among infected with HIV(25).

There are five TB outcomes: cure, treatment completion, treatment default, death, and treatment failure. The cure outcome refers to a patient who is smear-negative at, or one month prior to, the completion of treatment and on at least one previous occasion. In 1990, WHO chose 2015 as the target to cutting TB mortality and prevalence in half

Tuberculosis treatment success rate is the percentage of all new tuberculosis cases registered under a national tuberculosis control programme in a given year that successfully completed treatment, with or without bacteriological evidence of success ("cured" and "treatment completed" respectively)(26, 27).

Tb Burden

TB is one of the leading global infectious disease threats and is among the top 10 causes of death worldwide(1). Although an estimated 10 million developed TB in 2019 and 1.4 million died from TB-related illness(1, 28). In addition, increases in TB diagnosis and notification over the past decade have resulted in more people receiving TB treatment(29). Globally, 7.1 million people with TB were newly diagnosed and notified in 2019, up from 5.7 to 5.8 million annually in 2009 through 2012(1).

The WHO's End TB Strategy calls for a 90% reduction in TB deaths and an 80% reduction in incidence by 2030, compared to the 2015 baseline. The goals for 2020 are a 35% reduction in deaths and 20% reduction in incidence which are close to being met in Europe, where 31% decrease in deaths and 19% drop in incidence since 2015 has been noted. Africa has also made strides, with estimated death and incidence declines of 16% and 19% in the WHO African region respectively(30).

Covid-19 Impact On TB and Other Diseases

The COVID-19 pandemic has affected TB control programs and the incidence of catastrophic costs by distorting the health system at different levels. In general, the most noticeable effect is the prioritization for COVID-19–related healthcare services above other health problems. The prioritization has also resulted in a switch in roles of healthcare staff to COVID-19–related services that eventually have reduced the number of consultation services and the delivery of TB-related programs in either healthcare facility or community(31). The WHO reported that 122 countries have partially or entirely disrupted healthcare services for noncommunicable diseases(1). This could also reduce healthcare service availability for TB, as many TB-related resources are designated to COVID-19 services(32).

In the primary care level, the pandemic affected most health promotion and disease prevention programs. When physical distancing measures were promoted, primary healthcare facilities reduced TB-related health promotion programs, which are delivered in groups. Contact tracing was also affected because of a much more limited number of healthcare staff to do such programs including TB preventive therapy

that could increase the likelihood of secondary cases in households. Most TB-related services were also closed(33).

In some countries, TB-related services are provided in secondary care–level facilities. MDR TB services, including the diagnostic procedure, are also often delivered in hospital. With an increasing volume of COVID-19 cases in hospitals, TB-related services and its healthcare staff reduced which interrupted TB services in hospitals therefore causing an increase in patients' diagnostic delays(33).

One of modalities to reduce TB diagnostic delay is the rapid GeneXpert device. However, because of the pandemic and the vast need to identify SARS-CoV-2 virus, some countries encouraged the use of GeneXpert to test suspected COVID-19 patients. For COVID-19 control, this initiative boosts the COVID-19 testing scale but also reduced the TB test capacity, particularly for countries that rely heavily on the GeneXpert device (Cepheid, Sunnyvale, CA). It would, therefore, hinder the identification of TB cases and increase its diagnostic delay(33).

The diagnostic delay and not notified cases also aggravated by patient avoidance of healthcare services, in particular public healthcare services that were linked to the National Tuberculosis Program (NTP) and now commonly designated for COVID-19 services. Avoidance comes from a real concern that visiting such healthcare services may increase the risk of being infected by COVID-19(34, 35).

More than 50% of TB patients in Kenya and India feared contracting COVID-19 at a health facility(33). Their avoidance of the already reduced TB-related services led to a higher number of interrupted TB treatments or even to patients being lost to follow-up. Patients who have interrupted TB treatment usually face prolonged TB treatment. Patients who are lost to follow-up may face more severe symptoms, fail to complete their treatment, undergo category 2 TB treatment (i.e., TB treatment received by patients who have failed treatment, lost to follow-up, or recurrence), or even (multi)drug-resistant TB. The above outcomes increase the risk of hospitalization and more expensive treatment; two conditions that are risk factors for catastrophic costs due to TB(35).

For drug-resistant TB patients, the pandemic causes a much more complicated situation. They still need to visit a hospital, where such care is often delivered, with much higher caution from either themselves or healthcare staff to prevent the COVID-19 infection. If a patients' concern of contracting COVID-19 leads to limitations in accessing MDR-TB treatment, the risk of a more severe condition, longer treatment period, hospitalization, or extensively drug-resistant TB increase. All will result in a higher cost and risk of experiencing catastrophic costs or impoverishment(33).

Tuberculosis patients and their families are known to spend unnecessary costs on diagnostic tests, consultation, and hospitalization(34, 36). The fear of visiting healthcare facilities because of COVID-19 reduced such unnecessary costs. The pandemic also raised awareness of respiratory disease symptoms and encouraged people to seek care for respiratory complaints. In some cases, this reduced diagnostic delay of TB and prevented unnecessary costs in the pre-diagnostic phase(33).

The COVID-19 pandemic also caused an economic recession that significantly impacted household financial capacity because of the rise in unemployment rates and the decrease of income(37). The loss of jobs, income reduction, and poverty are risk factors for catastrophic costs due to TB(38).

Poor households that faced unemployment and substantial income loss became forced to buy cheaper, less nutritious meals(39). This leads to poor nutrition in the long run. Poor nutrition is a risk factor for the development of TB and, if a patient receives TB treatment, it may negatively affect TB treatment(40). The treatment may be unsuccessful and need to be continued to a longer period. When the TB treatment is prolonged, it can increase the risk of catastrophic costs due to TB(33).

Factors associated with treatment outcomes

A study was done in India among 50 patients aged 21–40 years (50%) and 41–60 years (28.3%) followed for period of six months to observe the treatment outcome under the DOTS regime. The cure rate was significantly more among non-alcoholics compared to alcoholics. The cure rate was only 60% among smokers compared to 88.5% among non-smokers and this difference was found to be statistically significant. Smoking and alcohol were found to be important risk factors for treatment failure in that study(41).

A study done in Pakistan showed the treatment success rate of 67.8% among new, retreatment PTB patients and 69% in new smear positive PTB patients. 21% and 15.7% in PTB and new smear positive PTB patients had loss to follow-up during treatment respectively. Overall, older patients (AOR 1.02; 95% CI 1.01-1.0). smokers (AOR 1.65; 95% CI 1.02–2.67) and retreatment cases of TB (AOR 2.34; 95% CI 1.43–3.84) were at greater risk of having unsuccessful treatment outcomes. Sputum positivity at 2 months (AOR 13.78, 95% CI 5.09–37.26) was a significant predictor of poor treatment outcomes in new smear positive PTB patients. The treatment success rate among PTB patients was lower than the recommended 85% success rate(42).

A study done in Eastern Ethiopia to determine the factors associated with TB treatment outcome shows that the overall rate of the treatment success 92.5%. The treatment success rate was higher among females (93.8%) than males (91.6%) and patients from rural setting (94.4%) than urban setting (92.4%). The proportion of TB patients with treatment success steadily decreased since 2012 (94.8%), 2013 (93.9%), 2014 (93.0%), and 2015 (90.8%); however, the difference was no statistically significant (p-value = 0.429). the treatment success rates were 94.3%, 90.7% and 92.3% among the PTB Smear positive, PTB smear negative and EPTB patients, respectively. In the bivariate analysis, variables with P value of < 0.2 were sex, age, pretreatment weight, HIV status, patient category, and type of TB(43).

In the multivariable logistic regression, sex, age, pretreatment weight, HIV status, and TB Patient category were found to be independently and significantly associated with the treatment outcome. The chance of having successful TB treatment outcome was higher among the female patients compared to the male. The HIV negative patients had 6.60 times higher odds(43).

Barriers and facilitators of tb treatment outcome

Studies of patients' TB treatment success have identified socio-economic and structural barriers to treatment success, including lack of money to pay for transportation, high distance from clinics, the difficulties associated with daily treatment and rigid routines at health facilities (44–50). Inadequate knowledge about the illness was also found to adversely impact treatment success. The studies also showed that family support, involvement in TB clubs, and adequate knowledge about the disease were facilitators of TB treatment success. (49, 50)

Methods

Study design

Sequential explanatory mixed methods was used. A retrospective cohort study was employed for the quantitative component to answer objective 1.

A qualitative study with a phenomenology approach was adopted to get an in-depth understanding to the barriers and facilitators to treatment success during the COVID era among Tuberculosis Patients at Jinja Regional Referral Hospital. The lived experience of the TB patients who had participated in the quantitative component was captured.

Study setting

The study was conducted among TB patients at Jinja Regional Referral Hospital, a government hospital located in the Eastern Region of Uganda in the center of Jinja Town, not far from the source of the Nile. It is the Regional Referral Hospital for the eastern districts of Bugiri, Iganga, Jinja, Kaliro, Kamuli, Mayuge, Kayunga and part of Mukono. It is the largest hospital in eastern Uganda, with a bed capacity of 600 located at 00°25'52.0"N, 33°12'18.0"E (Latitude:0.431111; Longitude:33.205000) and registered 450 TB patients 2019 and 550 TB patients in 2020. The TB clinic operates every day from Monday to Friday offering all TB related services such as refill, counselling and referral among others. The TB clinic serves both the in and out patients in Jinja Regional Referral Hospital. The TB clinic has a general TB register for all registered patients attending treatment, an MDR register for MDR confirmed patients, and Patient TB cards.

Quantitative component

Populations

Target Population

TB patients attending treatment at Jinja Regional Referral Hospital in Jinja District.

Accessible Population

TB patients registered in the TB ward at Jinja Regional Referral in March 2019 to March 2020 and April 2020 to April 2021 whose data can be accessible.

Study Population

TB patients registered in the TB ward who started and completed treatment from March 2019 to March 2020 and April 2020 to April 2021who fulfilled the selection criteria

Selection criteria

Inclusion criteria

All confirmed TB patients registered in Jinja Regional Referral Hospital who started and completed treatment from March 2019 to March 2020 and April 2020 to April 2021 with a record of TB treatment outcome.

Exclusion criteria

Patients transferred to other facilities during this study period.

Sample size

Objective one

To determine the association between COVID-19 period and Tuberculosis treatment success among Tuberculosis Patients at Jinja Regional Referral Hospital, was estimated using the double population proportions formula.

A comparison of two proportion formula was used;

$$N = \frac{(Z_{1-\alpha/2}\sqrt{2\pi_1(1-\pi_1)} - Z_{\beta}\sqrt{\pi_1(1-\pi_1)+\pi_2(1-\pi_2)})^2}{(\pi_1 - \pi_2)^2}$$

$Z_{1-\alpha/2}$ is the standard normal corresponding with the 5% level of significance, 1.96

Z_{β} is the standard normal value corresponding with 80% power, 0.84

π_1 is the Proportion in the control group.

π_2 is the Proportion in the exposed group.

The health Sector performance report for 2019/2020 showed the treatment success rate for Jinja district decreased by 26 to 47% from 73% in FY 2018/19(9).

$\prod 1$ = 73% (Proportion of TB patients with TB treatment success rate in 2019)

$\prod 2$ = 47% (Proportion of TB patients with TB treatment success rate in 2020)

Zβ standard normal value corresponding to 1-Power of study (β = 0.2) = − 0.84

N = 48 patients

With a 10% adjustment for missing data, N = 54 TB patients

Total sample size will then be 54*2 = 108 TB patients

Sampling technique

I enrolled all participants available at the time of data collection who met the study eligibility criteria.

Study variables

Main exposure variable

Objective one: Pre-Covid era as of March 2019 to March 2020 and Covid era as of May 2020 to May 2021

Other exposure variables

Objective one: Sex, Age, nutritional status (Weight), HIV sero-status, distance from the health facility, type of TB, Prescribe regimen and DOTS.

Outcome Variable

Objective one: categorized as Treatment success and Treatment Failure. Treatment success had patients that Cured and Treatment completion while Treatment failure had those patients lost to follow and died.

Data collection

A data abstraction sheet was designed and used to extract the required data from the TB ward registers and double checked for accuracy using the Case based surveillance system for TB. The data was collected with the help of the TB ward data officer who served as the research assistant, A one-day orientation on the data abstraction sheet was done. We pretested the data abstraction sheet using 20 records of 2018 and they were not included in the analysis.

We retrieved records for patients at the TB ward from the TB register book for March 2019 to March 2020 and May 2020 to May 2021. The first two weeks of November 2021 were used for data collection in the hospital.

Data management

The data was cross-checked by the principal investigator to ensure correctness and completeness. The filled forms were transported in boxes to data entry room and kept in lockable cabinets accessible to only authorized personnel. The data was then be entered into Epi-data, Data was coded and cleaned for consistency and completeness, frozen and kept safely backed up in the external hard discs and kept in a computer with a password. A duplicate copy of the frozen data was exported to STATA version 14 for subsequent analysis.

Data analysis

Bivariate analysis

Relative Risk were used to measure association between the predictor variables and main exposure variable. The 95% confidence intervals were also computed, chi square test used to assess the association. The level of significance was 5% or all the tests. For independent variables with more than two levels, Modified Poisson regression was carried out to determine the Relative Risk.

Multivariate analysis

Multivariate analysis was used to identify the independent predictors and subsequently to assess for interaction and confounding. Factors with p-values <= 0.2 was considered for multivariate analysis and consistently known from literature.

Interaction was assessed using the chunk test and when there was no interaction then assessment for confounding was done.

Testing for interaction was done by forming interaction terms with the main predictors. The difference in the -2 LL of the full model and reduced model was done to show if there is interaction (The difference in the -2LL will not be significant if chi-square p-value>0.05). Testing for confounding was done by getting the difference in the RR for variables that were not interacting.

Quality control

- Errors in this study were minimized by training of the research assistant.
- The data abstraction sheet were pre-tested for validity at the hospital.
- The collected data was reviewed by the principal investigator by entering data in it.

Qualitative component

Study population

The study population was health workers working in the TB clinic and TB patients in Jinja district whose records would had been used in the quantitative component who accepted to provide a written informed consent.

Sample size estimation

The study enrolled 12 TB patients stratified by Sex, HIV status and treatment outcomes.

2 TB patients, 1 Male and 1 Female who cured during the COVID era and HIV negative.

2 TB patients, 1 Male and 1 Female who cured during the COVID era and HIV positive.

2 TB patients, 1 Male and 1 Female who didn't complete treatment during the COVID era and HIV negative.

2 TB patients, 1 Male and 1 Female who didn't complete treatment during the COVID era and HIV positive.

2 TB patients, 1 Male and 1 Female who had treatment completion but didn't cure during the COVID era and HIV negative.

2 TB patients, 1 Male and 1 Female who had treatment completion but didn't cure during the COVID era and HIV positive.

In addition, health care workers were interviewed until data saturation is achieved i.e., focal person of the JRRH TB services, 1 medical doctor, 1 Pharmacist, 1 Clinical Officer, 2 nurses, linkage facilitator and a counselor.

Sampling method

Purposive sampling was used with special interest in information rich participants.

The patients were varied by HIV status, sex and treatment outcomes.

Data collection procedures

In-depth interviews

The principal investigator trained 2 social scientists who had experience in qualitative research involving TB patients. During the study, after collecting the data from the patient registers, quantitative findings that needed further explanation were identified. In-depth interviews, guided by a pretested topic guide with probes (appendix II) were conducted.

In-depth interviews were conducted in Lusoga or English (appendix V or VI) and back translated by 2 expert translators into English for those in Lusoga and pre-tested on 5 TB patients on ward. The interviews took about 30 minutes on average. There was audio recording and note taking and interviews were conducted from the hospital private wing board room.

Key informant interviews

Key informant interviews were held on appointment with selected participants during the study.

The interviews were guided by a pre-tested interview guide to assess their views regarding the facilitators and barriers towards treatment success, and their suggestions on how treatment success can be improved. These interviews were conducted in English and also audio recorded.

Data management

Information obtained was transcribed and read through several times to ensure that the content was well transcribed i.e., responses complete, quality of transcripts and pattern of responses. Lusoga transcribed interviews were translated into English by Lusoga expert and exported to Open Code version 4.02, a Computer Aided Data Analysis Software (CAQDAS) for coding and analysis.

Data analysis.

Qualitative data from the interviews was all be transcribed into text format in Microsoft word document and that in Lusoga translated into English. Data was analyzed using deductive thematic method (51) for barriers and facilitators with the help of OpenCode version 4.02 software.

Two independent investigators (social scientists) with experience in qualitative research and the PI conducted the analysis. Each of them read the scripts separately and thereafter met and discussed areas of agreement and disagreement.

Both the results from the quantitative and qualitative were triangulated with a conceptual link. After interpretation, they were categorized with emergent themes using the behavior model of utilization as developed by Anderson (52).

Study findings were presented with direct quotations of the respondents.

Trustworthiness of the qualitative method

For credibility

During data collection, participants were told about the study, allowed to ask questions and consent before participation. This enabled us to get participants who offered the information freely.

Triangulation of qualitative data from at analysis, quantitative and qualitative data at discussion.

Two independent investigators (social scientists) with experience in conducting qualitative research and the PI conducted the analysis. They read the scripts separately and met thereafter to discuss areas of agreement and disagreement.

At the end of each interview, the researcher's interpretation of the participant's interview was told to the participant to enable verification of interpretation.

For transferability

The researchers provided a detailed description of the context in which the research was carried out, the setting, sample size, sample, sampling strategy, demographic and clinical characteristics, interview procedure and topics and excerpts from the interview guides.

For dependability and confirmability

Raw data (that is audio recordings, notes from interviews and transcripts) was named using unique codes to represent participants and the date of creation to enable confirmation of data analysis as well as interpretation. Notes on the development of codes and sub-themes was also be kept.

Reflexivity

The investigators had no relationship with the participants.

Notes on observations, emotions and responses were kept.

Results

Quantitative results

Between March 2019 to March 2020 126 TB patients were screened. Of these 110(87%) were enrolled in the study. Sixteen were not enrolled because they had been transferred to the MDR register. Between April 2020 to April 2021 124 were screened. Of these 118(95%) were enrolled in the study. Of these 6 were transferred to the MDR registerc.

Study population characteristics

Out of the 228 TB patients, more males 66/100(60.0%) were from the pre-Covid era compared to the 62/118(52.5) in the covid era. The population in these two populations were not different(P-value 0.286). Disease classification was not different among the two groups. There was no difference in age distribution between the two groups. Treatment mode and Treatment Outcome were statistically significant as show in Table 1 below.

Table 1
Socio-demographic and Clinical characteristics of 188 TB Patients in Jinja Referral Hospital

Characteristic	Pre-Covid (March 2019- March 2020) (N = 110)	After Covid (May 2020 -May 2021) (N = 118)	p-Value
Gender			
Male	66(60.0)	62(52.5)	0.286
Female	44(40.0)	56(47.5)	
Disease classification			
Pulmonary Bacterial Diagnosed TB	52(47.3)	67(56.3)	0.069
Pulmonary Clinically Diagnosed TB	55(50.0)	43(36.4)	
Extrapulmonary TB	3(2.7)	8(6.8)	
HIV status			
Negative	81(74.3)	85(72.0)	0.407
Positive	28(25.7)	33(28.0)	
Treatment mode			
Facility Dot	54(49.1)	20(16.9)	< 0.001
Digital Community Dot	31(37.3)	51(43.2)	
Non-Digital Community	15(13.6)	47(39.8)	
Treatment Outcome			
Completed	71(64.5)	38(32.2)	< 0.001
Cured	26(23.6)	56(47.5)	
Failure	3(2.7)	7(5.9)	
Death	10(9.1)	17(14.4)	
Age in Years			
≤ 35	67(60.9)	69(58.5)	0.708
> 35	43(39.1)	49(41.5)	
Weight in Kgs			
≤ 55	74(67.3)	87(73.7)	0.285

Characteristic	Pre-Covid (March 2019- March 2020) (N = 110)	After Covid (May 2020 -May 2021) (N = 118)	p-Value
> 55	36(32.7)	31(26.3)	
Distance from the facility			
Less than 5Km	23(20.9)	25(21.2)	0.959
Greater than 5km	87(79.1)	93(78.8)	

Table 2
Effect of Covid 19 Period on TB treatment success among patients in Jinja Regional Referral Hospital

Outcome	Pre-Covid-19 (N = 110)	After Covid-19 (N = 118)	P-Value
Treatment Success	97(88.2)	94((79.7)	0.081
Treatment Failure	13(11.8)	24(20.3)	

From the Table 2 above, the Covid period had no significant effect on TB treatment success

Association between COVID-period and TB Treatment Success

In the unadjusted analysis (Table 3), participants who received treatment during the COVID period compared to the Pre-Covid period were not significantly less likely to achieve TB treatment success (RR, 1.04, 95% CI, 0.78–1.38). However, Males compared to female were also not significantly more likely to achieve TB treatment success (RR, 1.02; 95% CI, 0.76–1.36), and those HIV Positive compared to HIV negative (RR, 1.00; 95% CI, 0.73–1.39) were not associated with TB treatment success.

Those older than 35 years compared to those less than 35 years (RR, 0.0.99; 95% CI, 0.74–1.33), were not associated with TB treatment success and those who stayed less than 5km from the facility compared to those who stay greater than 5km from the facility (RR, 0.89; 95% CI, 0.0.64–1.25) were not associated with TB treatment success.

After adjusting for age categories, Disease classification, HIV status, treatment mode, Weight categories and distance from the facility and level of health facility, our data showed none was significantly more likely to achieve TB treatment success.

Table 3
Predictors of TB treatment success

Characteristic	Treatment Success		Crude RR (95% (Confidence Interval)	p-Value
	Yes No			
	N (%) N(%)			
Treatment Period				
Before Covid	94(41.2)	24(10.5)	Reference	
After Covid	97(42.6)	13(5.7)	1.04(0.78–1.38)	0.791
Gender				
Male	109(47.8)	19(8.3)	1.02(0.68–1.23)	0.572
Female	82(36.0)	18(7.9)	Reference	
Disease classification				
Pulmonary Bacterial Diagnosed TB	106(46.5)	13(5.7)	Reference	
Pulmonary Clinically Diagnosed TB	75(32.9)	23(10.1)	0.92(0.68–1.23)	0.572
Extrapulmonary TB	10(4.4)	1(0.4)	1.13(0.59–2.15)	0.719
HIV Status				
Negative	142(62.6)	24(10.6)	Reference	
Positive	49(21.6)	12(5.2)	1.00(0.73–1.39)	0.979
Treatment mode				
Facility Dot	77(33.8)	15(6.6)	Reference	
Digital Community Dot	66(29.0)	8(3.5)	0.96(0.69–1.33)	0.795
Non-Digital Community	48(21.1)	14(6.0)	0.93(0.64–1.35)	0.700
Age in Years				
≤ 35	119(52.2)	17(7.5)	Reference	
> 35	72(31.6)	20(8.7)	0.99(0.74–1.33)	0.964
Weight in Kgs				
≤ 55	136(59.7)	25(11.0)	Reference	
> 55	55(24.1)	12(5.2)	1.05(0.77–1.33)	0.757
Distance from the facility				
Less than 5Km	147(64.5)	33(14.5)	Reference	

Characteristic	Treatment Success		Crude RR	p-Value
	Yes No		(95% (Confidence Interval)	
	N (%) N(%)			
Greater than 5km	44(19.3)	4(1.7)	0.89(0.64–1.25)	0.513

Table 4
Multivariate analysis

Characteristic	Treatment Success		Adjusted RR	p-Value
	Yes No		(95% (Confidence Interval)	
	N (%) N(%)			
Treatment Period				
Before Covid	94(41.2)	24(10.5)	Reference	
After Covid	97(42.6)	13(5.7)	1.05(0.77–1.45)	0.743
Gender				
Male	109(47.8)	19(8.3)	1.02(0.75–1.37)	0.921
Female	82(36.0)	18(7.9)	Reference	
Disease classification				
Pulmonary Bacterial Diagnosed TB	106(46.5)	13(5.7)	Reference	
Pulmonary Clinically Diagnosed TB	75(32.9)	23(10.1)	0.95(0.69–1.32)	0.497
Extrapulmonary TB	10(4.4)	1(0.4)	1.18(0.58–2.39)	0.648
HIV Status				
Negative	142(62.6)	24(10.6)	Reference	
Positive	49(21.6)	12(5.2)	1.01(0.72–1.41)	0.962
Treatment mode				
Facility Dot	77(33.8)	15(6.6)	Reference	
Digital Community Dot	66(29.0)	8(3.5)	0.93(0.66–1.33)	0.700
Non-Digital Community	48(21.1)	14(6.0)	0.89(0.57–1.40)	0.624
Age in Years				
≤ 35	119(52.2)	17(7.5)	Reference	
> 35	72(31.6)	20(8.7)	0.98(0.72–1.34)	0.922
Weight in Kgs				
≤ 55	136(59.7)	25(11.0)	Reference	
> 55	55(24.1)	12(5.2)	0.01(0.71–1.43)	0.972
Distance from the facility				
Less than 5Km	147(64.5)	33(14.5)	Reference	

Characteristic	Treatment Success		Adjusted RR	p-Value
	Yes No		(95% (Confidence Interval)	
	N (%) N(%)			
Greater than 5km	44(19.3)	4(1.7)	0.90(0.63–1.29)	0.577

Qualitative results

Seven key informant interviews were conducted in total. They included focal person of the JRRH TB services (Nursing officer),1 medical doctor, 1 Clinical Officer, 2 linkage facilitators and a counselor. Twelve in-depth interviews were carried out. The participants for the in-depth interviews were asked again to confirm their barriers and facilitators to seeking TB services during the COVID-19 Era. Details for the participates are shown in Table 4 below

Table 5
Characteristics of 12 participants of in-depth interviews at Jinja Regional Referral Hospital

No	Study ID	HIV status	Sex	Age	Residence	TB treatment Outcome
1	01	Negative	Male	25	Jinja Town	cured
2	02	Positive	Female	32	Namulesa	cured
3	03	Negative	Male	42	Mafubira	cured
4	04	Positive	Female	37	Bugembe	cured
5	05	Negative	Male	27	Walukuba	Didn’t complete treatment
6	06	Positive	Female	32	Wanyange	Didn’t complete treatment
7	07	Negative	Male	42	Wairaka	Didn’t complete treatment
8	08	Positive	Female	46	Mpumudde	Didn’t complete treatment
9	09	Negative	Male	25	Walukuba	Completed but didn’t cure
10	10	Positive	Female	38	Buikwe	Completed but didn’t cure
11	11	Negative	Male	34	Mafubira	Completed but didn’t cure
12	12	Positive	Female	29	Bugembe	Completed but didn’t cure

The facilitators and barriers to treatment success during the COVID era among Tuberculosis patients at Jinja Regional Referral Hospital were categorized at individual, health facility and community level(Table 5).

Table 6
Barriers to treatment success during the COVID era among Tuberculosis patients at Jinja Regional Referral Hospital.

Theme	Sub-theme	Related codes
A: Individual level factors	1. Inadequate health care information	fear coming to hospital, when they come to hospital they will be admitted, sometimes can't swallow drugs, Admission pauses their work, TB and HIV myth, We're fearing the COVID thing in the hospital, Lack of information in some communities,
	2. Financial constraints	Long distance between the patient and facility, Lack of transport, Transport to pick drugs and review,
	3. Life styles	Alcoholism, Forgetting to have refills,
B: Facility related factors	1. Accessibility of the Hospital	Long distance between the patient and facility,
	2. None government funding	Lack of funds to follow up on patients, None Government funding of TB programs, No allowances to patients and clinicians who work with TB patients,
	3. Few Health Workers	government hospital we get a lot of patients, we dont follow up on patients, we truck those lost to follow up,
3. Community factors	1.Fear of discrimination	Low self-esteem, No privacy to take drugs,
	2.Difficulty in follow up	Unreliable contacts for follow up
	3. Poor community attitudes and lack of support	Stigma, HIV patients have stigma, Issue of stigma, Found out that I have TB and they have started mistreating me

Theme A: individual level barriers to treatment success during the covid era.

Majority of the barriers mentioned were at the individual or intra personal level as shown by the subthemes below.

Inadequate health care information

Several of the participants lacked adequate health care information and this was a barrier to treatment success during the COVID era. They emphasized fear coming to hospital, when they come to hospital they will be admitted and We're fearing the COVID thing in the hospital

A participant noted "*some patients were fearing to come to hospital as they say once you go, you have covid, they test you for covid, and they were fearing that covid thing, they keep you for isolation for some*

good time and that one you find that our number reduced, from what we used to notify to a smaller number" (**HCW 3**)

Another participant noted *"They fear coming to hospitals, why they have that mentality that when they come to the hospital, they will be admitted"* **(HCW 4).**

Financial constraints

The participant revealed financial constraints in terms of general up keep, and transport costs due to the health facility being far.

One participant reported *"...it has been somehow hard for me in form of transport to come and pick the drugs"* **(ID=02)**

Another participant reported …*"most of the patients were not coming for the refill because of the difficulties in transport, cause it was cut off from public means and most of them come from long distance, so such patients were not accessing the refills, so some them were going to nearby health facilities for a refill, and some of them they could communicate they have been refilled from other facilities, others they could not until you try to find out, that's when they tell you we got from here others they never got a refill."* (**HCW 1**).

Life styles

Life style of alcoholism was linked to missing drug refills.

For instance, one health worker reported, "*...like we have patients who are in a certain area like mafubira, for them their daily meal is alcohol. So such patients they may forget that at all to have a refill on this a date, that I have to go back to the hospital to get more drugs and he may end up failing to come oba [or] missing oba [or] forgetting to come back*" (**HCW 7**)

Theme B: facility-based barriers to treatment success during the COVID era**.**

These barriers related to the health institutional barriers influencing treatment success during the COVID era among Tuberculosis patients at Jinja Regional Referral Hospital. These were mentioned mostly by the HCWs.

Few health care workers

All linkage facilitators expressed dissatisfaction with the health care workers being few which would in turn lead to prolonged waiting hours which was expressed as a major barrier. This barrier was further reiterated by the HCWs

For instance, one health worker reported "…..we have the lab people there very few whereby this is a referral hospital it has been getting most of that what of the numbers , so tb like, let me say like for

genexpert, you can have like a hundred samples one person is supposed to run all those samples moreover he not having only genexpert samples, so when there not they run some of the sample and leave the others hmm otherwords they don't run all the samples you guys request for sometimes work…….. **(HCW 2)**

Accessibility of the Hospital

The patients and health care workers expressed concerns about the accessibility of the hospital because this would lead to up giving since most patient had to move from far places to obtain drug refills and medical checkups.

One health care worker narrated *"….we got some challenges about these patients who are distant from the hospital, those who are far from the facility, there was a challenge of transport because you remember during covid times , transport whatever's were…, we were in lockdown so the transportation was a bit hard for some patients to come but a few managed to come"* **(HCW 4)**

" ….th*e long distance between a patient and a facility where he or she is getting treatment from, because we have patients who come from far,, let me say.. …kailro and he or she gets drugs from Jinja Regional Referral Hospital, such patients faced difficulty to move from the far place to the hospital since transport and movement was restricted during the lockdown…..*" **(HCW 2)**

None government funding

Some health workers pointed out that donors failed to support most of the TB activities as government redirected most of its funding to COVID-19 activities and neglected TB services.

"……*During this period, we practically stopped calling patients because of lack of funds. I was constantly worried about what the situation will be in a few more days and where I'll we be and how we should behave during this period. Since the outbreak of the virus, every day I was more worried and concerned about my family, my friends, the entire world. Always we were anxious and not functioning like we used to. We were more irritable and we don't feel like talking to anyone since most of our donors stopped supporting us, like we were not functioning well as the TB unit……".* **(HCW 5)**

Theme C: community level barriers to treatment success during the COVID era.

These barriers related to interpersonal relationships with the community in which the patients leave.

Fear of discrimination

One of the major mentioned barriers was stigma associated with HIV positive status, and TB. The patients reportedly feared being seen receiving TB drugs

from the health facility by someone who could know them who could then know their status. This made it difficult to utilize community drug delivery services in privacy.

"*…that musawo [Health Worker] you know at home when they found out that I have TB they started mistreating me, so I got that stigma of not taking drugs well, on time….(**ID=02)***

"…….if someone is having TB we wouldn't have in community and even some health workers think TB is transmitted in cups taking tea on cups which is wrong, get self from those infection that's even how I would pick it, from utensil……..ok " **(HCW 7)**

"*……there is a lot of stigma for TB even health workers themselves for instance some will not enter ward yet is a health worker reason as being once I enter there I will caught TB ..*"(**HW 7**)

Difficulty in follow up

There was reported difficulty in follow up reported because of lack of reliable information to follow up.

One health care worker said *"Follow up is a problem to these patients, being a referred, we receive those patients from different areas to our facility but they give us unreliable information to follow-up on them when they miss treatment."* **(HCW 7)**.

Poor community attitudes and lack of support

The TB patients as well as health care workers expressed poor community attitudes towards. It was noted that there was stigma in the community when it comes to TB.

"there is a lot of stigma for TB even health workers themselves for instance some will not enter ward yet is a health worker reason as being once I enter there I will caught TB" **(HCW 7***).*

Facilitators to treatment success during the COVID era.

Table 7. Facilitators to treatment success during the COVID era among Tuberculosis patients at Jinja Regional Referral Hospital

Theme	Sub-theme	Related codes
D: Individual level factors	1. Desire to protect family member	Protecting the people, I stay with
E: Facility related factors	1. Availability of drugs and services	Availability of drugs, drugs are always available, take drugs to the community, the drugs have been there,
	2. Counselling services	Counsel them,
	3. Good patient health worker relationship	Good care from the health worker, we do follow up on patients,
	4. Incentives	MDR patients with food and some transport money
	5. Presence of TB guidelines	Guidelines were always being updated,
	6. Quality services at the Hospital	Also give quality services, working as a team on the TB ward,
F: Community Factors	1. TB awareness programs	TB awareness

Theme D: individual level facilitators to treatment success during the COVID era .

Only one facilitator was mentioned at the individual level by the patients. This was desire to protect family members.

Desire to protect family members

Most of the TB patients mentioned the desire to protect their family members as a motivator.

One participant noted that "……*When I reach home from hospital, we sit together and talk…now we have more time…children have no school…earlier we sit and watch TV together… Every one in TV is talking about corona…how many died? How many are getting it mostly us who have TB…how they go from one hospital to hospital and then how they die… my friends also send many horrible things in messages…how corona can go inside heart, head and all… I am coming to hospital …so I show all this to doctors and nurses…they say that many things are not like this but I should continue with my drugs. So I take my drugs to protect the people I stay with……*" (**ID= 07**)

Theme E: health facility level facilitators to treatment success during the COVID era .

Availability of free drugs and services

Both the patients and health workers mentioned that there were no drug stock outs during the COVID era, their availability most of the time was a major motivator.

One participant noted "…..*You people have drugs……*" (**ID=04**)

Another participant noted "…..*During the pandemic, we could deliver, we could do drug community distribution , we take their drugs to their homes or we tell them like they could get center they stand there we take the drugs there…..*"*(***HW2***)*

Another participant noted ***"****….sometimes we run out of stock of some medicines for TB, but it is rare, so I cant say that we run out of stock for TB drugs, there always available…….*" (**HW4**)

Counselling

In-depth with the participants, revealed that support and counselling from Health workers.

"*…there some that have stigma, there some who don't and that come back to us we the health workers, before starting a patient on tb drugs, you have to counsel him or her and guide him or her relating to the society where they come from and there.. it is their duty or their role either to disclose or not to disclose ….*"**(HCW 1)**

Good patient Health worker relationship

Patients as well as the health workers voiced the ability to freely interact together as a major motivator.

One participant noted *"They treated very well, they gave me drugs, then prescribed for me and I started taking the medication, when I swallowed the drugs I didn't feel bad except that my urine had the colour like the drugs, so I asked then they told me it is supposed to be like that, then I was confortable….."* **(ID=02)**

Incentives

The provision of incentives such as food and transport refund encouraged patients to good treatment outcomes.

One participant noted "*We have even patients for MDR TB and we do provide them with something, we give food, we give some money to those who are specifically to those who are having MDR TB*'(**HW 6**)

Presence of TB guidelines

Another major motivator at the health facility level mentioned by the health worker was presence of TB guidelines.

One participant noted *"..they always updated us with more guidelines about tb services.."* (**HW3**)

Quality services at the hospital

"……most people who come here from other facility they believe this a center of excellence, am going to jinja regional referral hospital for treatment, so however much the distance is long and we were in a lockdown they try and come….." (**HCW 1**)

Theme F: community level facilitators to treatment success during the COVID era .

TB awareness programs

Living in communities where there were good reports about radio talk shows inviting patients to pick their drugs.

*One participant said ", most of the radios could talk about them, if your HIV positive go for your drugs, you have diabetes try to for your drugs, you're a TB patient go for your drugs, so they were motivated by the media" (**HW5**)*

Discussion

This study assessed the effect of the COVID-19 period on TB treatment success at the Jinja Regional Referral Hospital. We observed an overall decrease in of TB treatment success patient from 88.2–79.7% in the period of pre-covid to after the covid era thou this decrease was not significant with p-value of 0.081.

The observed overall no difference between the two periods can be attributed to updating the guidelines by Ministry of Health, TB awareness programs during the pandemic and community drug deliveries which in turn could have resulted into the observed overall no difference. As cited in the qualitative component, TB awareness programs, Availability of free drugs and Services and Presence of TB guidelines. Together these components could have resulted into continuity of TB services hence COVID period not effecting the TB treatment success.

Another participant noted "…..*During the pandemic, we could deliver, we could do drug community distribution, we take their drugs to their homes or we tell them like they could get center they stand there we take the drugs there….."(***HW2***)*

Another participant noted "*…. sometimes we run out of stock of some medicines for TB, but it is rare, so I cant say that we run out of stock for TB drugs, there always available…….*" (**HW4**)

One participant noted "..they always updated us with more guidelines about tb services.." **(HW3**)

One participant said ", most of the radios could talk about them, if your HIV positive go for your drugs, you have diabetes try to for your drugs, you're a TB patient go for your drugs, so they were motivated by the media" (HW5 *)*

The observed difference between the two periods by MoH could have been due to under-diagnoses or under-reporting are issues. This is similar to a study done in India to determine the impact of COVID-19(53). However, the continued access to TB diagnosis and care was ensured to mitigated the disruptions of the pandemic hence no observed difference between the two periods.

There is a scarcity of studies that have assessed the effect of COIVD-19 period on TB treatment success.

Factors associated with COVID-19 period and tuberculosis treatment success

Distance from the facility

There was no significant association between distance from the facility and TB treatment Success.

Our data show that the majority of people with TB travel longer distances to access treatment, and longer travel distance is associated with reduced TB treatment success. The finding that people with TB who travel long distances to access treatment have decreased TB treatment success is consistent with several studies (54-57). The distance from the facility was solved by notable interventions such as community drug delivery to address physical barriers during the covid as noted by a health worker *"…..During the pandemic, we could deliver, we could do drug community distribution , we take their drugs to their homes or we tell them like they could get center they stand there we take the drugs there….."*(**HW2**), hence no observed association between Distance from the facility and TB treatment success.

Weight

There was no significant association between weight and TB treatment Success.

Our results differ from those of a multi-site study, Treatment outcomes and factors associated with mortality among individuals with both TB and HIV in the antiretroviral era in Thailand (58).

It showed that weight is associated with an increased risk of death during TB treatment(59, 60). Malnutrition can suppress cell-mediated immunity, which represents the principal host defense against TB. Therefore, high mortality rates among underweight individuals with TB may be due to impaired immunity and, as a result, a more severe infection in this population (61).

Barriers to treatment success during the COVID-19 era

The qualitative findings revealed barriers at the individual, health facility and societal level.

Individual level barriers to treatment success during the COVID era

The major reported barrier at this level was financial constraints which were in terms of transport costs and inadequate health care information which made if difficult to come to the health facility. Other barriers reported were life styles as many patients restored to alcoholism.

A mixed methods cross sectional study carried out in India to characterize and address the socioeconomic impact of accessing TB diagnosis and care in Nepal showed barriers of Complementary to pills and tests, this socioeconomic support will be an essential part of eliminating TB by 2050(62).

Health facility-based barriers to treatment success during the COVID era

The major reported barrier at this level was few health care worked and non-government funding of TB Programs during the pandemic.

Across sectional study Anticipating the impact of the COVID-19 pandemic on TB patients and TB control programmes predicted that health workers would become few and most donors would reduce funding to TB services during the COVID-19(63-65)

Community level barriers to TB treatment success during the COVID-19 era

The major reported barrier was fear of discrimination, poor community attitudes and lack of support.

Tuberculosis stigmatization is a problem in many settings, though more so in LMICs. It rose and became confounded by COVID-19. Stigma is associated with fear, and fear of COVID-19 increased. This had be seen imported into Africa—with stigmatization being directed not only at the affected patients but also their careers and family. This applies equally to healthcare workers who are likely to be managing both COVID-19 and TB(63).

Facilitators to treatment success during the COVID-19 era

Individual level facilitators to treatment success during the covid-19 era

Desire to protect family members was one of the main facilitators to treatment success.

Desire to protect family members has been cited as the major facilitator to TB treatment success

Health facility level motivators treatment success during the COVID-19 era

Availability of free drugs and services, counselling and presence of TB guidelines, Updating of the MoH guildeness to support community drug delivery might have improved on the TB treatment success.

Community level facilitators to treatment success during the COVID-19 era

TB awareness programs helped to remind patients to get drug refills and this reduced on the effect of COVID-19 Period on TB treatment success.

Strengths of the study

- This was a sequential explanatory mixed methods study which helped us gain a better understanding of effect of COVID-19 on TB treatment success in Jinja Regional Referral Hospital.
- We applied the WHO standard definitions to define our outcomes thus reducing erroneous assignment of treatment outcomes to the study participants.
- Both the qualitative and quantitative components were done by well trained nurses and social scientists.

Limitations of the study

- This study had a potential for selection bias as it was in one regional referral Hospital the population obtained may not be an accurate representation of TB Patients in Uganda. Furthermore, the study had few HIV Positive patient that had sought treatment in the selected period thus the potential for selection bias.
- The study was conducted in primarily a rural setting so the findings might not be generalizable to urban settings.
- The researchers being part of the TB health care ecosystem are in a strong position to understand and interpret the context. However, the possibility of personal bias and power bias cannot be ruled

out.

- Purposive selection of participants and its potential for judgment bias, use of practical objective interview guides instead of a previously validated instrument and not exploring personality traits that play a role in how a patient responds to drugs are the limitations of the study.
- Although data about sputum smear conversions were verified using the laboratory register to ascertain cure, we used routine data in the TB unit registers which may be prone to errors and missing values encountered in routine care settings in resource-limited settings.
- We did not have access to standard measures of HIV disease progression, namely viral load, CD4 counts, access to ART, and hospitalization rates among others. This is a limitation in our analysis because these factors drive mortality among persons with TB. Our study also assumed that mortality resulted from TB. However, the exact cause of death in this study is not known.

Conclusions

COVID – 19 period had no effect on TB treatment success at Jinja Regional Referral Hospital. Although no statistically significant, at Treatment outcome level COVID-19 had an impact on the different treatment outcomes.

A number of facilitators and barriers influenced TB Treatment Success among TB patients at Jinja Regional Hospital among the patients at an individual, health facility and community level. The major barriers mentioned were few health care workers, financial constraints, inadequate health care information, life styles, discrimination and poor community attitudes and lack of support. The major facilitators were good relationship with health care workers, TB awareness programs, updating of TB guidelines and availability of free drugs and services.

That said, these findings have important implication on the improving the TB guidelines in Uganda to improve treatment success. This study has the opportunity to support MoH on the ongoing End of TB in Uganda. Measures towards alleviating fear and stigma and ensuring financial securities of the patients during the time of health crisis are important for preparedness against epidemics such as COVID-19.

Recommendations

For policy

Taken cautiously, findings from this study support wider updating of the TB treatment guidelines by MoH especially to cover for future Pandemics in Uganda.

For practice

There is also need for MoH to support health care workers involved in the provision of TB services by training more HCWs.

The hospital administration and supporting partners like should emphasize counselling for TB patients and community drug delivery.

For research

Future researchers should consider use of prospective research methods to determine the effect of COVID-19 on TB treatment success by studying patients who had coinfection of TB and COVID-19.

Abbreviations

AFB	Acid-Fast Bacilli
AHSPR	Annual Health Sector Performance Report
COVID-19	Corona Virus Disease 2019
DOTS	Directly Observed Treatment, Short-course
DST	Drug susceptibility testing
EPTB	Etra Pulmonary Tuberculosis
FY	Financial Year
HIV	Human immunodeficiency virus
JRRH	Jinja Regional Referral Hospital
MDR-TB	Multidrug-resistant tuberculosis
MOH	Ministry of Health
NTLP	National Tuberculosis Leprosy Program
NTRL	National Tuberculosis Reference Laboratory
PTB	Pulmonary TB
PI	Principal investigator
SARS	Severe Acute Respiratory Syndrome
TB	Tuberculosis
TSR	Treatment Success Rate
WHO	World Health Organization

XDR-TB Extensively drug-resistant tuberculosis

Declarations

Ethics approval and consent to participate

Permission to conduct the study was obtained from the Clinical Epidemiology Unit, Makerere University, college of Health sciences. Ethical approval was obtained from the Makerere University College of Health sciences School of Medicine Research Ethics Committee (SOMREC).

Written informed consent forms was obtained from eligible participants. Consent forms were translated into a language they are comfortable with. Study serial numbers will be used instead of names to maintain confidentiality. The data was coded and only accessible to the study team. TB patients with failure treatment Outcomes were encouraged to continue attending TB services at the facility.

Permission for waiver of consent was obtained from Makerere University College of Health sciences School of Medicine Research Ethics Committee (SOMREC).

Acknowledgement

Clinical Epidemiology Unit especially, Jinja Regional Referral hospital especially the TB ward team and the participants for their tremendous help.

Contributors

JH collected the data, performed the analysis, wrote the report , drafted the manuscript, guaranteed and accepted full responsibility for the work and/or the conduct of the study, had access to the data, and controlled the decision to publish. AK and EM extensively supervised the entire research process, reviewed the report and manuscript and gave final approval for submission and publication.

Funding

The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests

None declared.

Patient and public involvement

Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Provenance and peer review

Not commissioned; externally peer reviewed.

Data Availability statement

Data sharing is applicable for all datasets generated and/or analysed for this study.

Patient consent for publication

Not applicable.

Ethics approval

Ethical clearance for the study was issued by the higher degrees, research and ethics committee of Makerere University School of Public health. An ethical approval ID was not obtained since board does not issue IDs to master students' approved research. Participants who gave their opinions signed a written informed consent before participating. Participants gave informed consent to participate in the study before taking part.

References

1. WHO. Global tuberculosis report 2020: World Health Organization; 2020 [Available from: https://www.who.int/publications/i/item/9789240013131.
2. Aturinde A, Farnaghi M, Pilesjö P, Mansourian A. Spatial analysis of HIV-TB co-clustering in Uganda. BMC Infect Dis. 2019;19(1):612.
3. Adepoju P. Tuberculosis and HIV responses threatened by COVID-19. Lancet HIV. 2020;7(5):e319-e20.
4. Abdool Karim Q, Abdool Karim SS. COVID-19 affects HIV and tuberculosis care. Science. 2020;369(6502):366–8.
5. Kadota JL, Reza TF, Nalugwa T, Kityamuwesi A, Nanyunja G, Kiwanuka N, et al. Impact of shelter-in-place on TB case notifications and mortality during the COVID-19 pandemic. Int J Tuberc Lung Dis. 2020;24(11):1212–4.
6. Bhargava A, Shewade HD. The potential impact of the COVID-19 response related lockdown on TB incidence and mortality in India. Indian J Tuberc. 2020;67(4s):139-s46.
7. Uganda MoH. Ministry of Health coronavirus: MOH; 2021 [Available from: https://www.health.go.ug/covid/.
8. Adigun R, Singh R. Tuberculosis. StatPearls. Treasure Island (FL): StatPearls Publishing Copyright © 2021. StatPearls Publishing LLC.; 2021.
9. MOH. ANNUAL HEALTH SECTOR PERFORMANCE REPORT FINANCIAL YEAR 2019/20. 2021.

10. Izudi J, Semakula D, Sennono R, Tamwesigire IK, Bajunirwe F. Treatment success rate among adult pulmonary tuberculosis patients in sub-Saharan Africa: a systematic review and meta-analysis. BMJ Open. 2019;9(9):e029400.
11. Konwloh PK, Cambell CL, Ade S, Bhat P, Harries AD, Wilkinson E, et al. Influence of Ebola on tuberculosis case finding and treatment outcomes in Liberia. Public Health Action. 2017;7(Suppl 1):62-s9.
12. Malik AA, Safdar N, Chandir S, Khan U, Khowaja S, Riaz N, et al. Tuberculosis control and care in the era of COVID-19. Health Policy Plan. 2020;35(8):1130–2.
13. Desta KT, Kessely DB, Daboi JG. Evaluation of the performance of the National Tuberculosis Program of Liberia during the 2014–2015 Ebola outbreak. BMC Public Health. 2019;19(1):1221.
14. MOH. National Guidelines for Management of Covid-19. In: Health Mo, editor.; 2020.
15. McQuaid CF, McCreesh N, Read JM, Sumner T, Houben R, White RG, et al. The potential impact of COVID-19-related disruption on tuberculosis burden. Eur Respir J. 2020;56(2).
16. Roberts L. Why measles deaths are surging - and coronavirus could make it worse. Nature. 2020;580(7804):446–7.
17. Riley T, Sully E, Ahmed Z, Biddlecom A. Estimates of the Potential Impact of the COVID-19 Pandemic on Sexual and Reproductive Health In Low- and Middle-Income Countries. Int Perspect Sex Reprod Health. 2020;46:73–6.
18. Ekuka G, Kawooya I, Kayongo E, Ssenyonga R, Mugabe F, Chaiga PA, et al. Pre-diagnostic drop out of presumptive TB patients and its associated factors at Bugembe Health Centre IV in Jinja, Uganda. Afr Health Sci. 2020;20(2):633–40.
19. Raviglione M, Sulis G. Tuberculosis. 2015: Burden, Challenges and Strategy for Control and Elimination. Infect Dis Rep. 2016;8(2):6570.
20. Shretta R, Liu J, Cotter C, Cohen J, Dolenz C, Makomva K, et al Malaria Elimination and Eradication. In: Holmes KK, Bertozzi S, Bloom BR, Jha P, editors. Major Infectious Diseases. Washington (DC): The International Bank for Reconstruction and Development / The World Bank © 2017 International Bank for Reconstruction and Development / The World Bank.; 2017.
21. Bloom BR, Atun R, Cohen T, Dye C, Fraser H, Gomez GB, et al Tuberculosis. In: Holmes KK, Bertozzi S, Bloom BR, Jha P, editors. Major Infectious Diseases. Washington (DC): The International Bank for Reconstruction and Development / The World Bank © 2017 International Bank for Reconstruction and Development / The World Bank.; 2017.
22. Rieder HL. Reflections on the end TB strategy. Indian J Tuberc. 2019;66(1):167–9.
23. Chopra KK, Arora VK. End TB - Strategy - A dream to achieve. Indian J Tuberc. 2019;66(1):163–4.
24. Izudi J, Tamwesigire IK, Bajunirwe F. Surveillance for multi-drug and rifampicin resistant tuberculosis and treatment outcomes among previously treated persons with tuberculosis in the era of GeneXpert in rural eastern Uganda. J Clin Tuberc Other Mycobact Dis. 2020;19:100153.

25. MOH. UGANDA NATIONAL TUBERCULOSIS. AND LEPROSY CONTROL PROGRAMME Revised Strategic Plan 2015/16–2019/20. 2017(JUNE 2017).
26. Akanbi K, Ajayi I, Fayemiwo S, Gidado S, Oladimeji A, Nsubuga P. Predictors of tuberculosis treatment success among HIV-TB co-infected patients attending major tuberculosis treatment sites in Abeokuta, Ogun State, Nigeria. Pan Afr Med J. 2019;32(Suppl 1):7.
27. Chaves Torres NM, Quijano Rodríguez JJ, Porras Andrade PS, Arriaga MB, Netto EM. Factors predictive of the success of tuberculosis treatment: A systematic review with meta-analysis. PLoS ONE. 2019;14(12):e0226507.
28. Tadolini M, García-García JM, Blanc FX, Borisov S, Goletti D, Motta I, et al. On tuberculosis and COVID-19 co-infection. Eur Respir J. 2020;56(2).
29. WHO. WHO Guidelines Approved by the Guidelines Review Committee. WHO consolidated guidelines on drug-resistant tuberculosis treatment. Geneva: World Health Organization © World Health Organization 2019.; 2019.
30. Chakaya J, Khan M, Ntoumi F, Aklillu E, Fatima R, Mwaba P, et al. Global Tuberculosis Report 2020–Reflections on the Global TB burden, treatment and prevention efforts. International Journal of Infectious Diseases. 2021.
31. Gurung SC, Dixit K, Rai B, Caws M, Paudel PR, Dhital R, et al. The role of active case finding in reducing patient incurred catastrophic costs for tuberculosis in Nepal. Infect Dis Poverty. 2019;8(1):99.
32. McKibbin W, Fernando R. Economics in the Time of COVID-19 (Issue May). CEPR Press; 2020.
33. Stop TB, Partnership. The Impact of COVID-19 on the TB Epidemic: A Community Perspective 2020. TB Affected Community Led Survey; 2020.
34. Rosenbaum L. The Untold Toll - The Pandemic's Effects on Patients without Covid-19. N Engl J Med. 2020;382(24):2368–71.
35. Fuady A, Houweling TAJ, Mansyur M, Burhan E, Richardus JH. Cost of seeking care for tuberculosis since the implementation of universal health coverage in Indonesia. BMC Health Serv Res. 2020;20(1):502.
36. Prasanna T, Jeyashree K, Chinnakali P, Bahurupi Y, Vasudevan K, Das M. Catastrophic costs of tuberculosis care: a mixed methods study from Puducherry, India. Glob Health Action. 2018;11(1):1477493.
37. Blustein DL, Duffy R, Ferreira JA, Cohen-Scali V, Cinamon RG, Allan BA. Unemployment in the time of COVID-19: A research agenda. J Vocat Behav. 2020;119:103436.
38. Fuady A, Houweling TAJ, Mansyur M, Richardus JH. Catastrophic total costs in tuberculosis-affected households and their determinants since Indonesia's implementation of universal health coverage. Infect Dis Poverty. 2018;7(1):3.
39. Brief P. The Impact of COVID-19 on Food Security and Nutrition. United Nations; 2020.

40. Samuel B, Volkmann T, Cornelius S, Mukhopadhay S, MejoJose, Mitra K, et al. Relationship between Nutritional Support and Tuberculosis Treatment Outcomes in West Bengal, India. J Tuberc Res. 2016;4(4):213–9.
41. Sreenivasulu T, Jahnavi K, Sreenivasulu T. A cross sectional study on factors affecting treatment outcome among TB patients. Int J Adv Med. 2018;5(1):175.
42. Masood R, Muhammad IN, Siddiqui T, Mushtaque M, Irshad A. High prevalence of DR-TB (drug-resistant tuberculosis): An Indicator of public health negligence. Pak J Pharm Sci. 2019;32(4):1529–36.
43. Woldeyohannes D, Assefa T, Aman R, Tekalegn Y, Hailemariam Z. Predictors of time to unfavorable treatment outcomes among patients with multidrug resistant tuberculosis in Oromia region, Ethiopia. PLoS ONE. 2019;14(10):e0224025.
44. Sagbakken M, Frich JC, Bjune G. Barriers and enablers in the management of tuberculosis treatment in Addis Ababa, Ethiopia: a qualitative study. BMC Public Health. 2008;8:11.
45. Demissie M, Getahun H, Lindtjørn B. Community tuberculosis care through "TB clubs" in rural North Ethiopia. Soc Sci Med. 2003;56(10):2009–18.
46. Michael KW, Belachew T, Jira C. Tuberculosis defaulters from the "dots" regimen in Jimma zone, southwest Ethiopia. Ethiop Med J. 2004;42(4):247–53.
47. Shargie EB, Lindtjørn B. Determinants of treatment adherence among smear-positive pulmonary tuberculosis patients in Southern Ethiopia. PLoS Med. 2007;4(2):e37.
48. Tekle B, Mariam DH, Ali A. Defaulting from DOTS and its determinants in three districts of Arsi Zone in Ethiopia. Int J Tuberc Lung Dis. 2002;6(7):573–9.
49. Getahun H, Aragaw D. Tuberculosis in rural northwest Ethiopia: community perspective. Ethiop Med J. 2001;39(4):283–91.
50. Demissie M, Kebede D. Defaulting from tuberculosis treatment at the Addis Abeba Tuberculosis Centre and factors associated with it. Ethiop Med J. 1994;32(2):97–106.
51. Patton MQ. Qualitative Research. Encyclopedia of Statistics in Behavioral Science2005.
52. Babitsch B, Gohl D, von Lengerke T. Re-revisiting Andersen's Behavioral Model of Health Services Use: a systematic review of studies from 1998–2011. Psychosoc Med. 2012;9:Doc11.
53. Migliori GB, Thong PM, Alffenaar JW, Denholm J, Tadolini M, Alyaquobi F, et al. Gauging the impact of the COVID-19 pandemic on tuberculosis services: a global study. Eur Respir J. 2021;58(5).
54. Wondale B, Medihn G, Teklu T, Mersha W, Tamirat M, Ameni G. A retrospective study on tuberculosis treatment outcomes at Jinka General Hospital, southern Ethiopia. BMC Res Notes. 2017;10(1):680.
55. Gabida M, Tshimanga M, Chemhuru M, Gombe N, Bangure D. Trends for tuberculosis treatment outcomes, new sputum smear positive patients in Kwekwe district, Zimbabwe, 2007–2011: a cohort analysis. J Tuberculosis Res. 2015;3(04):126.
56. Gebreegziabher SB, Bjune GA, Yimer SA. Total Delay Is Associated with Unfavorable Treatment Outcome among Pulmonary Tuberculosis Patients in West Gojjam Zone, Northwest Ethiopia: A

Prospective Cohort Study. PLoS ONE. 2016;11(7):e0159579.

57. Asres A, Jerene D, Deressa W. Tuberculosis treatment outcomes of six and eight month treatment regimens in districts of Southwestern Ethiopia: a comparative cross-sectional study. BMC Infect Dis. 2016;16(1):653.
58. Gatechompol S, Kawkitinarong K, Suwanpimolkul G, Kateruttanakul P, Manosuthi W, Sophonphan J, et al. Treatment outcomes and factors associated with mortality among individuals with both TB and HIV in the antiretroviral era in Thailand. J Virus Erad. 2019;5(4):225–30.
59. Yen YF, Tung FI, Ho BL, Lai YJ. Underweight increases the risk of early death in tuberculosis patients. Br J Nutr. 2017;118(12):1052–60.
60. Lai H-H, Lai Y-J, Yen Y-F. Association of Body Mass Index with Timing of Death during Tuberculosis Treatment. PLoS ONE. 2017;12(1):e0170104-e.
61. Cegielski JP, McMurray DN. The relationship between malnutrition and tuberculosis: evidence from studies in humans and experimental animals. Int J Tuberc Lung Dis. 2004;8(3):286–98.
62. Dixit K, Rai B, Prasad Aryal T, Mishra G, Teixeira de Siqueira-Filha N, Raj Paudel P, et al. Research protocol for a mixed-methods study to characterise and address the socioeconomic impact of accessing TB diagnosis and care in Nepal. Wellcome Open Res. 2020;5:19-.
63. Togun T, Kampmann B, Stoker NG, Lipman M. Anticipating the impact of the COVID-19 pandemic on TB patients and TB control programmes. Ann Clin Microbiol Antimicrob. 2020;19(1):21-.
64. Crisan-Dabija R, Grigorescu C, Pavel CA, Artene B, Popa IV, Cernomaz A, et al. Tuberculosis and COVID-19: Lessons from the Past Viral Outbreaks and Possible Future Outcomes. Can Respir J. 2020;2020:1401053.
65. Can Sarınoğlu R, Sili U, Eryuksel E, Olgun Yildizeli S, Cimsit C, Karahasan Yagci A. Tuberculosis and COVID-19: An overlapping situation during pandemic. J Infect Dev Ctries. 2020;14(7):721–5.

Appendices

Appendices are not available with this version.