Asian Journal of Probability and Statistics

Volume 23, Issue 2, Page 42-52, 2023; Article no.AJPAS.100520
ISSN: 2582-0230

Survival Patterns of Human Immunodeficieny Virus-Tuberculosis (HIV-TB) Co-Infected Patients in Selected Counties in Kenya

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

Article Information

DOI: 10.9734/AJPAS/2023/v23i2501

Open Peer Review History:
This journal follows the Advanced Open Peer Review policy. Identity of the Reviewers, Editor(s) and additional Reviewers, peer review comments, different versions of the manuscript, comments of the editors, etc are available here: https://www.sdiarticle5.com/review-history/100520

Original Research Article

Received: 15/04/2023
Accepted: 09/06/2023
Published: 28/06/2023

Abstract

One nation with a significant burden of tuberculosis and the human immunodeficiency virus is Kenya. Coinfection with tuberculosis and the human immunodeficiency virus/acquired immunodeficiency syndrome complicates infection control and lowers survival rates. While research on HIV/TB coinfection has been done in Kenya, little is known about the patterns in people's survival with Antiretroviral Therapy (ART) and T.B. therapy, particularly regarding the country's many Counties. This study used the Kaplan-Meier function to determine the trends in patient survival for those receiving ART and T.B. treatment in Kenya. A retrospective cohort research design was employed in the investigation. Patients receiving co-therapy for T.B. and ART management who visited the medical institutions between January 1, 2015, and December 31, 2019, were included in the target population. The National AIDS & STIs Control Program (NASCOP) database (secondary data) records of all HIV-TB co-infected individuals from the chosen counties in Kenya were used

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to create the study's sample. The survival function was estimated using the Kaplan-Meier estimator. According to the study, the use of ART and T.B. treatment statistically affects the survival of patients co-infected with HIV and T.B. More persons with T.B. and HIV infections who received both ART and T.B. treatment survived longer than those who received only ART up to about the 750th day. The study also discovered that the mortality rates for HIV-TB patients between 2015 and 2019 differed from county to county. The study also showed that throughout five years, there were variations in the distribution of T.B. and HIV mortality among the 47 Counties. The overall number of T.B. and HIV deaths in the 47 countries was 1077 in 2015. This figure fell to 921 in 2016, 391 in 2017, 106 in 2018, and 60 in 2019. Conclusion: Starting treatment later in the course of the disease may have a bigger impact on lowering T.B./HIV-related mortality than focusing interventions in the first few months following ART initiation.

Keywords: Immunodeficiency; antiretroviral therapy; endurance survival.

1 Introduction

1.1 HIV and T.B. coinfection

Since HIV and tuberculosis (T.B.) are both diseases that commonly affect persons with weakened immune systems, such as HIV-positive people, they are closely related [1]. People without HIV with low CD4 counts are substantially more vulnerable to active T.B. (when T.B. infection results in sickness). In contrast, people with good immune systems may not get sick from latent T.B. infection (when a person has T.B. but shows no symptoms). As a result, it is thought that HIV-positive people have a larger risk of getting active T.B. than HIV-negative people [2]. Low CD4 count HIV-positive individuals have a substantially higher risk of developing T.B. infection than HIV-negative individuals [3]. Nevertheless, early detection and adequate treatment are crucial to stop TB-related mortality.

T.B. surpassed HIV in 2014 as the largest infectious disease killer in the world, a concerning development for a generally curable and treated condition. In 2017, 1.3 million people died from T.B., while another 300,000 HIV-positive individuals perished. It remains the major cause of death for HIV-positive people [1]. Globally, 11% of people with HIV/TB coinfection died while undergoing treatment in 2017, over three times the rate of other T.B. patients (4%). TB-related deaths among HIV-positive individuals decreased by 100,000 between 2015 and 2017, primarily due to the quick uptake of antiretroviral HIV treatment. This indicates that progress has been made in lowering these deaths. Mohammed, Assefa & Mengistie, [4] investigated the prevalence of extrapulmonary tuberculosis among those with HIV/AIDS in sub-Saharan Africa using a thorough literature assessment. Google Scholar and PubMed were used to find published literature on extrapulmonary T.B. (EPTB) prevalence among people living with HIV/AIDS (PLWHA). According to the findings, 6.4% to 36.8% of PLWHA had EPTB. Consequently, it was thought crucial that medical professionals emphasize extrapulmonary T.B. testing, particularly when screening for T.B. among PLWHA. Mukuku et al., [5] investigated the coinfection of HIV and tuberculosis in young Congolese people. The study addressed kids under 15 and used a cross-sectional study design. The study discovered a 20.95% prevalence of HIVTB coinfection. HIV-infected children had a greater mortality rate for T.B. infections (47.73%) than HIV-uninfected children (17.02%). Nyamogoba et al. [6] used a cross-sectional study design in Kenya to examine HIV coinfection with tuberculosis and non-tuberculosis mycobacteria in western Kenya. According to the findings, of the 346 instances of T.B., 76% were HIV positive, and 41.8% were HIV negative but still had T.B. The prevalence ratio (P.R.) of TB-HIV coinfection in females was 1.35. The frequency of TB-HIV coinfection in Nyando Sub-County was 69.80%, according to a study conducted by Achieng' [7] on the parameters related to tuberculosis treatment results in TB/HIV co-infected and T.B. alone patients.

1.2 Survival of patients on antiretroviral therapy (ART) and T.B. treatment

Ji, Liang & Sheng, [8] used the Kaplan-Meier method to conduct retrospective cohort research on the mortality of HIV-infected patients with pulmonary tuberculosis in China. The findings showed that the total death rate over a median follow-up of 27 months was 15.92%. Risk factors for poor survival include age greater than 60, complications from bacterial pneumonia, delayed diagnosis, a low CD4+ T cell count of less than 50/mm3, and pulmonary atelectasis. In patients who had not started cART before beginning anti-TB therapy, it was

discovered that starting cART later (more than eight weeks after beginning anti-TB therapy) increased the mortality rate. In contrast, starting cART within 4- 8 weeks of anti-TB therapy was linked to the fewest deaths (0/14).

Zenner, Abubakar & Conti, [9] investigated how T.B. affected HIV-positive people's survival in England, Wales, and Northern Ireland. The study population comprised adults over 15 who received an HIV diagnosis between 2000 and 2008. The findings showed that individuals with T.B. and HIV coinfection accounted for 18% of the 1880 fatalities during follow-up and 79% of deaths the year after HIV diagnosis. Increased all-cause mortality was substantially correlated with T.B. coinfection. An analysis of AIDS-related survival revealed similar findings. The unanticipated high mortality rate among HIV-TB patients in a population with easy access to healthcare and ART availability emphasizes the significance of improving the identification of active and latent T.B. cases among HIV patients and HIV testing among T.B. patients to ensure appropriate and prompt treatment initiation for both diseases. Additionally, Keet [10] showed that even after successful T.B. therapy, HIV infection increases the mortality risk associated with tuberculosis. People with HIV and tuberculosis diagnoses were the study's target population, and a descriptive research design was used to conduct the investigation. About 10% of the 1,051 patients with T.B. who received an anti-TB and HIV prescription during their initial visit had passed away after five years, as opposed to less than 6% of those without T.B.. In contrast to individuals who had not had T.B. at the beginning of the study, more than 19% of participants co-infected with T.B. and HIV at their initial clinic visit had passed away after ten years.

In Brazil, [11] used a cross-sectional study methodology to investigate common anti-TB therapy regimens. He contends that while current anti-TB therapy regimens have an average 86% cure rate, HIV-positive patients experience worse outcomes than uninfected ones. Even while most HIV-infected patients react to anti-tuberculosis treatment (ATT) successfully at first, there is a high chance of contracting additional opportunistic infections and recurrent T.B., which increases mortality. Antiretroviral therapy (ART) should be started soon to improve these patients' long-term outcomes and lower death. Ji, Liang & Sheng, [8] used the Kaplan-Meier method to calculate survival rates at the start of ART. The study used a retrospective follow-up study design with 3598 individuals who were co-infected. According to the findings, patients with T.B. and HIV coinfection had survival rates of 82.0% at five years and 58.1% at ten years. Within ten years of starting ART, two out of every five TB-HIV patients died. Those receiving second-line ART, those with low baseline CD4 counts, and bedridden patients should be given more attention by current HIV prevention and treatment programs. Roshanaei et al. [12] examined the survival rates of patients co-infected with the human immunodeficiency virus and tuberculosis in Iran. Using Cox regression analysis, they found that coinfection with HIV significantly lowers the survival rate of T.B. patients, with a death rate of 20.7 times higher than that of TB-infected individuals alone.

Tshitenge, Ogunbanjo & Citeya, [13] used a cross-sectional study approach to examine the mortality of HIV-positive and tuberculosis-positive patients in Mahalapye, Botswana. The findings showed that the majority of patients with both T.B. and HIV were receiving antiretroviral therapy (ART) (81.63%) or had begun cotrimoxazole preventative therapy (CPT) (87.2%) while receiving anti-TB medication. Seventy-three (13.6%) individuals with T.B. and HIV coinfection passed away before finishing anti-TB therapy. Two patients on ART for at least three months before starting anti-TB treatment were among the three-quarters (74.4%) of patients who passed away before finishing anti-TB therapy. The majority (87.7%) of patients with T.B. and HIV coinfection started taking CPT before they passed away. This study proved that patients with T.B. and HIV coinfections had a 13.6% T.B. mortality rate. A substantial death rate was seen in those who did not take ART for the first three months and those who did not start CPT for the second and fifth months.

Manosuthi et al., [14] investigated the survival rates of HIV/tuberculosis co-infected individuals in Thailand with and without antiretroviral medication. The findings showed that survival rates among HIV/TB co-infected patients getting ART were 96.1%, 94.0%, and 87.7% at one, two, and three years following T.B. diagnosis, compared to 44.4%, 19.2%, and 9.3% among patients not receiving ART, respectively. Isolated pulmonary T.B., cervical tuberculosis lymphadenitis, isoniazid resistance, and multi-drug resistant tuberculosis (MDR-TB) were more prevalent in the ART group of patients. According to the Cox proportion hazard model, multi-drug resistant T.B. and gastrointestinal T.B. were linked to increased death, while ART was linked to lower mortality. Antiretroviral therapy significantly lowers mortality in HIV/TB co-infected patients, and starting ART within six months after T.B. diagnosis is linked to improved survival, according to this study. Similar research was done [15] on treating tuberculosis in people co-infected with the human immunodeficiency virus. The hazard

ratio (H.R.) of mortality for each variable at baseline and an estimation of the impact of risk variables among T.B. patients were calculated using the Cox proportional-hazards regression and log-linear model, respectively. The results showed that HIV coinfection was the cause of death in 50% of TB/HIV patients. During the extension care phase, the risk of death was noticeably higher in T.B. patients who were HIV-positive. Patients with T.B. and HIV receiving antiretroviral medication have a lower survival rate. HIV-positive individuals have a much lower chance of surviving T.B. Significant effects of age, weight, smoking, and alcohol have also been reported. Compared to mortality, failure, and default rates, which were recorded as 10.33%, 1.24%, and 8.65%, respectively, treatment success rates, cure rates, and treatment completion rates were higher in Nyando Sub-County, according to a study [7].

2 Methodology

2.1 Data

Secondary data from the National AIDS and STI's Control Programme (NASCOP) programs database was used in this investigation. Kenya's Ministry of Health uses NASCOP and National Land Transport Programme (NLTP), respectively, for regular case-based monitoring and reporting rules for HIV and T.B. For Kenyan healthcare facilities, NASCOP provides an Integrated Electronic Medical Records (EMR) Data Warehouse Integrated Development of Wildlife Habitats (IDWH) that houses HIV/AIDS-related information. Kenyan medical establishments must update their EMR databases in IDWH every month. The Tuberculosis Information from Basic Unit (TIBU), a case-based surveillance system with real-time reporting capabilities, has been hosted by NLTP. Since it was founded in 2012. With the help of TIBU, notifications for T.B. patients are now prompt and immediate, making it simple to generate reports. All Kenyan healthcare facilities, both public and private, are mandated to record information about cases of tuberculosis in the TIBU system. The national surveillance system and all of Kenya's counties' health facilities employ the same WHO data recording and reporting criteria as the NLTP and NASCOP programs. January 1, 2015, and the last day of 2019 were the study's five-year data points for each patient per county. The secondary NASCOP databases were obtained using a data extraction tool for the study. Treatment compliance was measured by the patient's consumption of the prescribed medications at the proper dosage and timing. Examining the patient attendance data at T.B. "sub clinics" and ART clinics. The lead researcher also reviewed the observed data on the likelihood that latent T.B. will advance to active T.B. Data on treatment outcomes also calculated the degree of adherence.

The researcher employed multiple regression imputation to address the issue of missing data, if any were present.

2.2 Kaplan meier curves

This study focuses on the relationship between time and an event, such as death. Data is censored in the following categories: alive if the subject made it to the cut-off date of December 31, 2019, lost to follow, or default up if the patient could not be located. Right Censoring was used in this study, which implies that although individuals were no longer being watched before they passed away, each one was at least kept under observation for a short period, allowing for the collection of some information regarding each subject's survival. The survival function S(t), which is the likelihood that a patient survives longer than time t, was estimated in the study using the Kaplan-Meier (K-M) method [16]. This strategy uses data from participants who have experienced an event and right-censored subjects, which favors the Kaplan-Meier approach in the survival analysis.

2.2.1 Survivor function

In the Survivor mode, the likelihood that a person will live for a time, t, greater than or equal to t is expressed as S(t). Depending on the study's objectives, any sample of survival data can be collected, taking censoring into account. For instance, the survivor function estimates for a given single sample of survival times without Censoring are given by,

(t) = Number of individuals with survival times ≥ t/Number of individuals in the data set.

S(t) = 1 −F(t)

Where; S(t);

The likelihood that a person will live for some time equal to or longer than t is known as S(t).

The ratio of the total number of participants in the study to the total number of individuals alive at time t is known as F(t). The survival time of an individual can take on any value, which can be written as; tT, and can take different values of the random variable T forming a probability distribution. Let t be the time until an event of interest occurs, and T be the entire period the experiment is supposed to last.

The distribution function of T is provided if we assume that the random variable T has a probability distribution with a density function f (t);

F(t) = P(T t) = int_ 0 tf(u)du.We can now define survivor function s(t) as the probability that an individual survival time is larger than or equal to t and is provided by; S(t) = P(T t) = 1 F (t). This is the likelihood that the survival time is smaller than some value t, where survivor time is the likelihood that a person lives from the beginning of the research to a point after t.

2.2.2 Censoring

When we know of the subject's event time but not the precise event time, censorship is said to be present. When the end point of interest is not observed, a participant's survival time in a study is said to have been censored. It may be right, left, or interval censoring.

If a subject starts the study at a time, t, indicated by t_0, and the occurrence of interest is noticed at an unknown time, t, then the subject's survival time, t, was; t_0+ t.

We refer to time, c, as the censored survival time if the subject lasted up until sometime, c, after entering the study, let's say t_0+ c, but may have vanished before time, t_0 + t, when the event of interest is seen.

If we let T represent failure time and C represent censoring time, then;

When a subject encounters the relevant event before the study officially begins, this is known as left Censoring. An individual's true survival time is shorter than what has been observed. Mathematically, it is written as T (0, c_1). It is known that only the failure time T is shorter than the censoring time cl that has been seen, but its precise value is unknown.

Right Censoring is when an individual may encounter the relevant event after a predetermined time t, but we only know that they are alive (and haven't failed) up to the study's end. The failure time is expressed mathematically as T (c_r), and the only thing known about it is that it is longer than the observed censoring time Cr. However, the precise value of the failure time cannot be observed.

When a specific event occurs in a certain period, it is the only available information (known as interval filtering). The failure time is only known to be more than the observed left censoring time, c I, and less than the measured right censoring time, c_r, mathematically, but the exact value cannot be determined.

3 Results and Discussion

3.1 Survival trends of patients on ART and T.B. treatment

The study aimed to determine the trends in patient survival in Kenya while receiving antiretroviral therapy (ART) and T.B. treatment. The Kaplan- Meier Estimate of the Survivor Function was used to determine the survival patterns of patients in Kenya receiving antiretroviral therapy (ART) and T.B. treatment. In the five years following the start of ART, 2,555 (7.9%) individuals infected with both T.B. and HIV in Kenya were confirmed deceased. The average period of the event's occurrence (death) was 1420 days for the group receiving both ART and T.B. treatment, according to the mean survival time for the event (dead) cases, which was 1420.328 (range 1399.206-1441.450). Most fatalities happened before 1617 days of therapy, as shown by the median survival time of 1617 days for the event (dead) cases. Additionally, the mean survival time for the event (dead) cases among people receiving ART solely was 1560.704 (range 1700-1799), indicating that the average

time the event occurred (death) was 1560 days. Most deaths occurred before 1617 days of treatment, according to the median survival time of 1750 days for the event (dead) patients.

Table 1. Means and medians for survival time

ART and T.B. treatment	Mean[a]				Median			
	Estimate	Std. Error	95% Confidence Interval		Estimate	Std. Error	95% Confidence Interval	
			Lower Bound	Upper Bound			Lower Bound	Upper Bound
ART and T.B. treatment	1420.328	10.777	1399.206	1441.450	1617.000	18.454	1580.829	1653.171
ART Treatment Only	1560.704	15.606	1530.116	1591.291	1750.000	25.427	1700.163	1799.837
Overall	1458.906	8.975	1441.314	1476.498	1646.000	17.469	1611.760	1680.240

3.2 The kaplan -meier curve

Fig. 1 Kaplan-Meier curve demonstrates that patients with T.B. and HIV infections who had ART and T.B. therapy had longer survival times than those with T.B. and HIV infections who received ART only up to about 750th day. Following that, those receiving ART alone outlived those receiving ART and T.B. treatment by a long margin. The World Health Organization states that a combination of antimicrobial drugs can treat active T.B. disease for six to twelve months. Isoniazid INH is frequently used with rifampin, pyrazinamide, and ethambutol to treat active T.B. However, the course of treatment for drug-resistant T.B. lasts 20 to 30 months or roughly 900 days. This demonstrates that everyone with both T.B. and HIV finishes their T.B. treatment in less than 900 days. As a result, none of the patients are receiving T.B. therapy beyond this time.

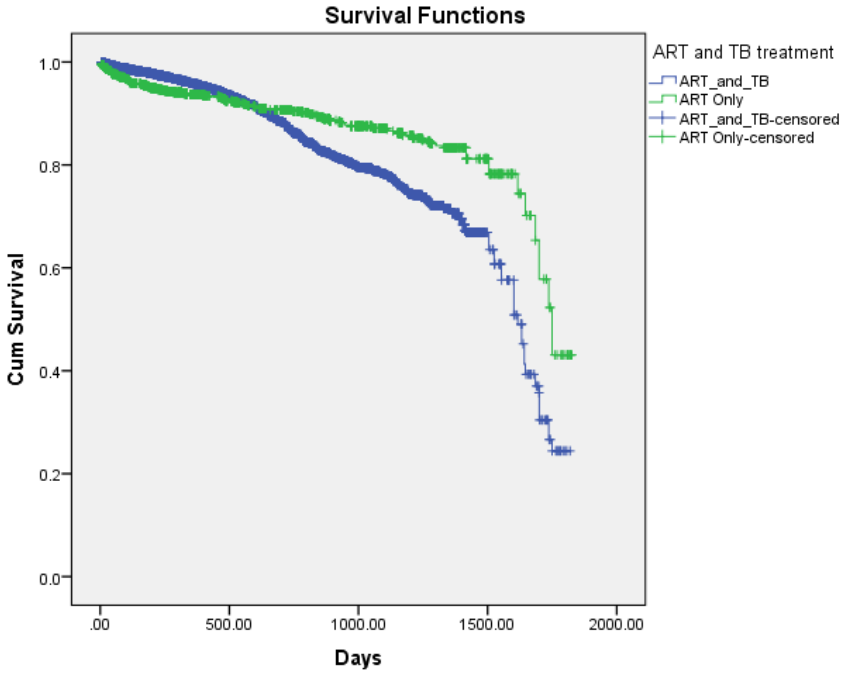

Fig. 1. Kaplan- meier curve for treatment and outcome

Fig. 2 Kaplan-Meier curve for marital status and the outcome demonstrates that separated and married polygamous people had low survival rates throughout the period. Minors had a modest chance of surviving, whereas monogamous singles and married people had a high chance. The cohabiting individuals' survival rates were high for the first 1.5 years, after which they started deteriorating.

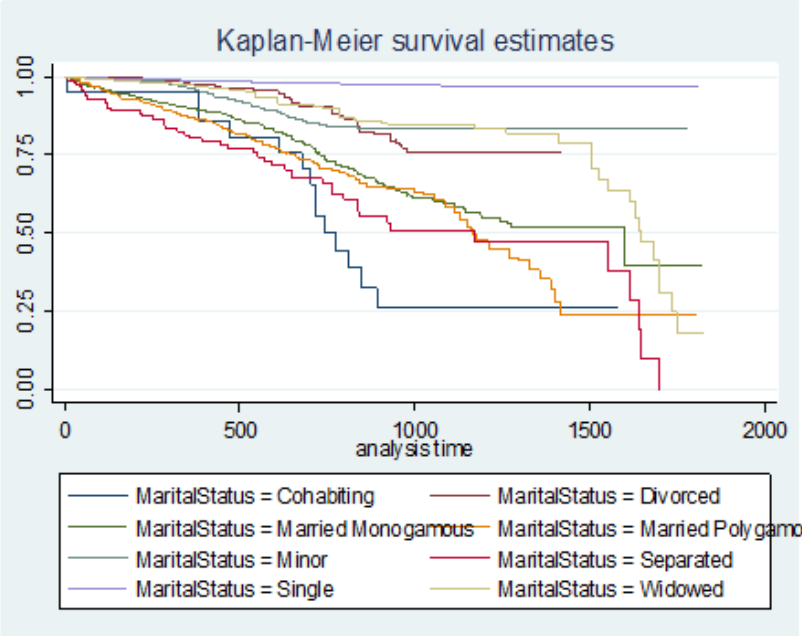

Fig. 2. Kaplan- meier curve for marital status and outcome

People in WHO clinical stage one had the highest survival rates, followed by those in stages two and three. The WHO clinical stage four patients had the lowest rates of survival.

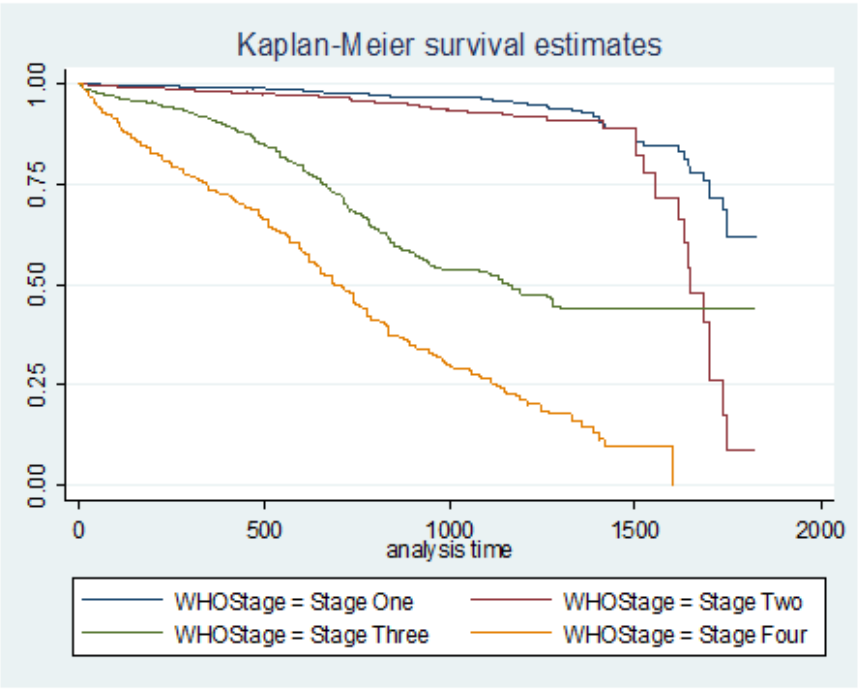

Fig. 3. Kaplan- meier curve for WHO stage and outcome

According to the findings displayed in Fig. 4, level 3 facilities had the lowest survival rates, followed by level 2 and level 5 facilities. People with HIV-TB coinfections had the lowest survival rates in level 4 facilities.

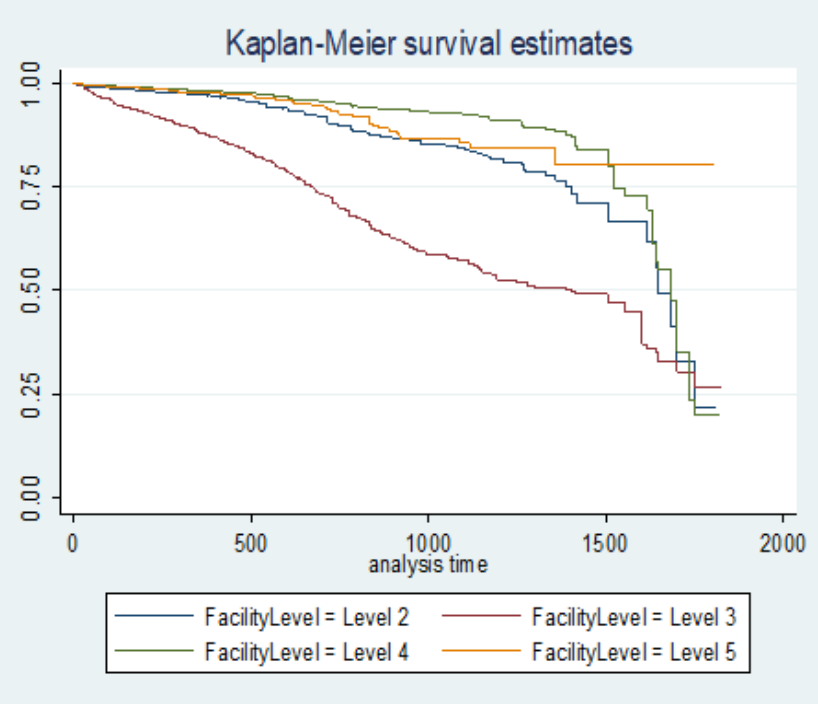

Fig. 4. Kaplan- meier curve for facility level and outcome

Patients co-infected with HIV and T.B. did not have significantly different survival rates in the first two years. The third year, however, marks a change, with the Nairobi region having the lowest survival rate, followed by the central and coastal regions. However, the Eastern region, followed by the North Easter region, had the highest survival rate.

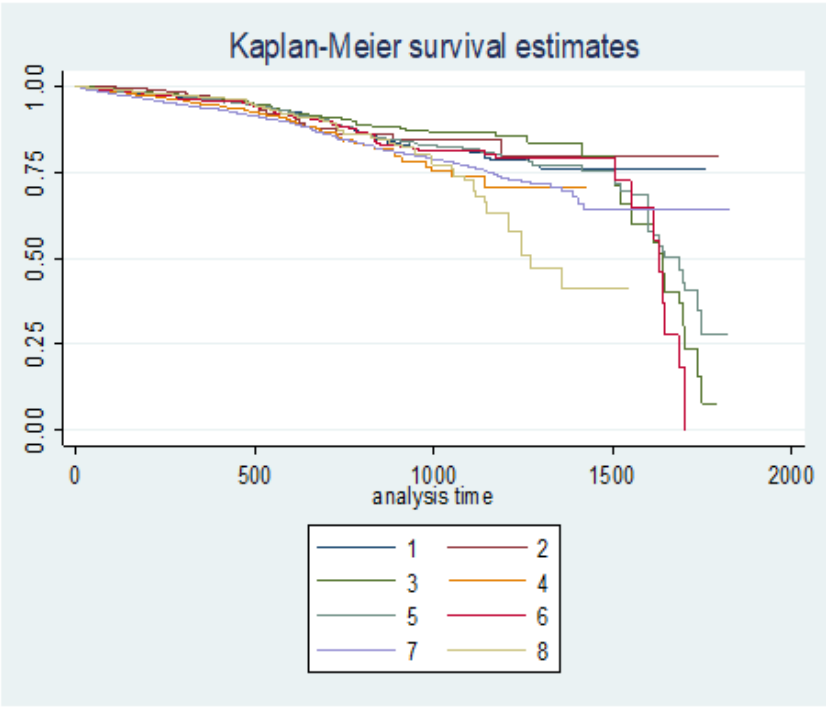

Fig. 5. Kaplan- meier curve for county and outcome

3.3 Discussion

3.3.1 Survival trends of patients on ART and T.B. treatment

The study's primary goal was to determine the trends in patient survival in Kenya receiving both ART and T.B. treatment. The outcomes showed that the two curves—ART alone and ART plus T.B. therapy combined—were statistically significantly different. This demonstrates how the use of ART and T.B. therapy statistically affects the survival of patients who are co-infected with HIV and T.B. According to the study, 7.9% of Kenyans with HIV and T.B. infection were reported dead five years after starting ART. Ji, Liang, and Shen [8] observed that the total mortality rate in China was 15.92% using the Kaplan-Meier technique. Ji, Liang, and Shen [8] discovered that the median follow-up length in China was 27 months using the Kaplan-Meier method.

Additionally, Keet [10] noted that after five years, 10% of patients with T.B. who were also provided anti-TB and HIV drugs on their initial visit had passed away, as opposed to 6% of those without T.B. The results support the claim made by Zenner, Abubakar, and Conti [9] that patients with T.B. and HIV coinfection accounted for 18% of the 1880 fatalities that occurred during follow-up and 79% of the deaths that occurred in the year after HIV diagnosis. The unexpectedly high mortality rate among HIV-TB patients in a population with easy access to healthcare and ART availability emphasizes the significance of improving the identification of active and latent T.B. cases among HIV patients and HIV testing among T.B. patients to ensure appropriate and prompt treatment initiation for both diseases. The average period of the event's occurrence (death) was 1420 days for the group receiving both art and T.B. treatment, according to the mean survival time for the event (dead) cases, which was 1420.328 (range 1399.206-1441.450). Most fatalities happened before 1617 days of therapy, as shown by the median survival time of 1617 days for the event (dead) cases.

Additionally, the mean survival time for the event (dead) cases among people receiving ART solely was 1560.704 (range 1700-1799), indicating that the average time the event occurred (death) was 1560 days. Most deaths occurred before 1617 days of treatment, according to the median survival time of 1750 days for the event (dead) patients. The results showed that patients with T.B. and HIV infections who had ART and T.B. therapy had longer survival times than those with T.B. and HIV infections who received ART just up to about 750th day. Following that, those receiving ART alone outlived those receiving ART and T.B. treatment by a long margin. The World Health Organization states that a combination of antibacterial drugs can treat active T.B. disease for six to twelve months. Isoniazid INH is frequently used with rifampin, pyrazinamide, and ethambutol to treat active T.B. However, the course of treatment for drug-resistant T.B. lasts 20 to 30 months or roughly 900 days. This demonstrates that everyone with both T.B. and HIV finishes their T.B. treatment in less than 900 days. As a result, none of the patients are receiving T.B. therapy beyond this time. Antiretroviral therapy (ART) started promptly has been demonstrated to lower mortality and enhance long-term outcomes for these patients, according to Swaminathan [11].

4 Conclusions and Recommendations

4.1 Conclusions

According to the study's findings, the use of ART and T.B. treatment statistically affects patients co-infected with HIV and T.B. in terms of survival. More persons with T.B. and HIV infections who received both ART and T.B. treatment survived longer than those who received only ART up to about the 750th day. Following that, those receiving ART alone outlived those receiving ART and T.B. treatment by a long margin. In the 47 Counties, the distribution of T.B. and HIV deaths changed over five years. The findings showed that weight and age greatly impacted HIV-TB confections.

4.2 Recommendations

According to the study, ART and T.B. treatment impacted the survival of HIV and T.B. patients in Kenya. Compared to starting therapy later in the course of the disease, focusing interventions in the first few months after ART initiation may have a stronger impact on lowering T.B./HIV-related mortality. The study suggests that the Ministry of Health should emphasize the combination of ART and T.B. therapy more to decrease the number of deaths, as some patients were not receiving ART and T.B. treatment.

The study suggests that the Ministry of Health emphasizes the coinfection of T.B. and HIV through the National AIDS & STIs Control Program (NASCOP) and National Tuberculosis Leprosy & Lung Disease Program. Significant T.B. and HIV mortality were reported in this study, and Kisii, Homa Bay, and Migori were identified as hotspots. To ensure that there is a decrease in the mortality of T.B. among HIV patients, there is a need for targeted intervention in these Areas.

Consent

As per international standard or university standard, respondents' written consent has been collected and preserved by the author(s).

Competing Interests

Authors have declared that no competing interests exist.

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