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ANALYSIS OF SURVIVAL PATTERNS OF TB-HIV CO-INFECTED PATIENTS IN RELATION TO TIMING OF ART INITIATION IN KIAMBU COUNTY, 2012-2016

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ABSTRACT

Background: TB-HIV co-infection remains a glaring challenge particularly in low resource countries.

The end TB strategy is focused towards the reduction of all TB related mortality by 95% by 2035

Objective: To analyze the survival patterns of TB-HIV co-infected patients in Kiambu County

Design: Retrospective cross-sectional study

Setting: Kiambu County, Kenya

Subjects: TB-HIV co-infected patients that were newly diagnosed with both tuberculosis and HIV infection.

Results: A total of 1,189 patients were included for the study. Tuberculosis was more prevalent among males 635 (53.4%) than females 554 (46.6%).The age group most affected was between 24-35 years. Gatundu zone had the highest number of TB-HIV co-infected cases notified. There was a general decline in the total number of TB-HIV co-infected patients reported across 2012-2016. Mortality was highest at <14 days 38.2%, followed by 15-30days 32.2%, 30-60days at 18.1% and was least in more than 60 days at 10.7% with ART initiation.

Conclusion: Survival of newly diagnosed TB and HIV co-infected patients in Kiambu County was noted to improve when ART was initiated 14 days after TB treatment commencement.

INTRODUCTION

Tuberculosis-Human Immunodeficiency virus (TB-HIV) co-infection poses a double challenge globally particularly in low resource settings. In 2014, an

estimated 1.2 million people that had tuberculosis globally were diagnosed with HIV infection, 74% of these were from Sub-Saharan Africa (1). Kenya, a low-middle income country (LMIC) is ranked 15th among the 22Tuberculosis (TB) high burden

countries (1). Of all the cases notified for TB in 2015 in Kenya, 93% had a HIV test done of which 31% were TB-HIV co-infected (2). Among those co-infected, only 74% were put on Antiretroviral therapy (ART) (2). Kiambu County is a moderate burden county for tuberculosis and high burden County for HIV/AIDS. The TB case notification in 2014 was 240/100,000, HIV prevalence of 3.8%, TB-HIV co-infection rate of 32% and an ART uptake of 87%. One of the impact targets of the Kenya National Health Sector Strategy Plan (KHSSP, 2014-2017) is to eliminate communicable conditions through reduction of the burden of communicable diseases until they are no longer a public health concern (3). One of the outcome indicators is to increase the treatment success rate in TB-HIV co-infected patients to 85% and reduce the case fatality of TB-HIV to less than 5% (4). Similarly, the End TB strategy targets to reduce deaths attributable to TB by 95% by the year 2035 (5). There is limited data on Tuberculosis mortality in Kenya. In 2015, it was estimated that the treatment success rate among the TB-HIV co-infected patients was 81.5% with a case fatality rate of 11% (2). ART initiation improves clinical outcomes in TB-HIV co-infected patients (6–10) by augmenting the immune system resulting in reduction of the mortality rate among TB/HIV co-infected patients. In Kenya, according to the national TB guidelines, a TB-HIV co-infected patient is to be initiated on anti-retroviral therapy (ART) within 14 - 56 days of starting TB treatment (11). However, the recently released ART guidelines, encourage the start of anti-retroviral therapy soonest the TB-HIV co-infected patient is able to tolerate the medication. In this study, we aim to analyze the characteristics and survival patterns in relation to the timing of ART treatment among TB-HIV co-infected patient.

MATERIALS AND METHODS

Study Design: A retrospective cross-sectional study using data generated in the Tuberculosis Information of Basic Unit at County level.

Study site and setting: Kiambu County is one of the 47 counties in Kenya with a population of about 1.7 million. It borders Nairobi County (one of the highest TB burden in Kenya) (4). It is divided into 12 sub-counties namely Thika, Gatundu North, Gatundu South, Juja, Ruiru, Githunguri, Kiambu, Kiambaa, Kikuyu, Kabete, Limuru and Lari.

In Kiambu County, there are a total of 364 health facilities across the County. Of these, there is one level 5 hospital (Thika level 5 hospital) which offers teaching (undergraduate students) and referral services, 3 level 4 hospitals which offer tertiary medical services, 20 high volume health centers which offer partial tertiary services and 54 dispensaries which offer basic medical services. The remaining 287 comprises of private clinics, private hospitals, faith based hospital and nursing homes. Of these, there are 131 TB treatment sites and 76 diagnostic sites. Some 47 facilities of these offer TB-HIV services under one roof. In regards to TB-HIV management, all TB treatment sites in the County offer Direct Counselling and Testing (DTC). As a policy guideline, this is mandatory for all the TB notified TB patients. In health facilities that provide both TB and HIV services, treatment for both conditions is done under one roof at no cost to the patient. This eases the patient movement in the facility, makes it easier for patient follow-up and reduces chances of defaulting from care. However, in health facilities that do not offer HIV treatment, the patient is linked to the nearest health facility for further management.

Study Participants: TB-HIV co-infected patients registered in TIBU (an electronic platform of data collection of TB patients in Kenya) in Kiambu County from 2012 to 2016. The population that was eligible for analysis was 1,189. This incorporated patient that were diagnosed to have tuberculosis and HIV infection for the first time.

The eligible population was calculated after eliminating the following populations: The population that was HIV negative, those with missing HIV and ART test dates, those who began TB treatment before 01/01/2012, those who ART treatment started before TB treatment, those who were transferred out, lost to **Analysis and data preparation**. Data was downloaded from TIBU and exported into an excel database using STATA® version 13 software. All analyses were conducted using STATA® version 13. Categorical data were described using frequencies, graphs, proportions and mean (\pm SD) for continuous data. Survival patterns were assessed using the Kaplan Meir curve. Variables with p-values less than 0.10 in the univariate analysis were included in the multivariate logistic regression model. All tests were two-tailed, and p-values less than 0.05 were considered statistically significant.

Ethical consideration: This study was approved by the Moi University College of Health Sciences (MU/CHS) and Moi Teaching & Referral Hospital (MT&RH) Institutional Review Board (IREC).

RESULTS

Records of 1,189 TB-HIV co-infected patients were analyzed. Males had a higher TB notification at 635(53.4%) than females. Most of the patients received TB care and treatment in the public sector 750(72.1%) compared to private and prisons. as shown in Table 1. Majority of the patients were normally nourished. Follow-up and those who were still on treatment.

Source of data: TB Program utilizes TIBU data management as central database of the National Tuberculosis and Lung Disease-Program which is a web based solution integrated with mobile/tablet technology developed and introduced in Kenya in the year 2012 with inter-sector support. Patients with TB upon diagnosis, are notified, treated and followed up with primary record capture obtained from patient records and Multidrug Drug Resistance log book entered into registers as a summary of the data entered in the registers. This data is subsequently uploaded at Sub – County level into TIBU by sub-county TB coordinators electronically via mobile computer tablets.

Table 1:

The socio, demographic and clinical characteristics of TB-HIV patients in Kiambu County, Kenya, 2012-2016

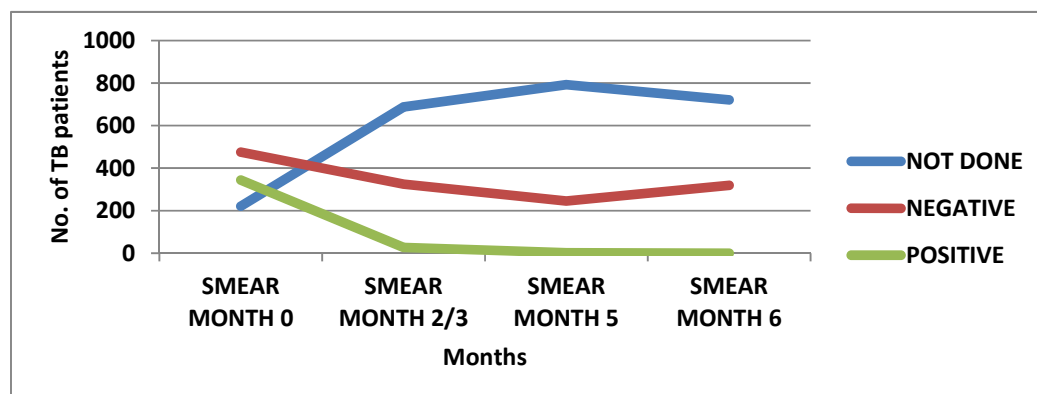
Characteristics		TREATMENT OUTCOME		
		CURED	DEAD	TOTAL
Sector (n=1,189)	Prisons	2 (0.2)	1 (0.7)	3(0.3)
	Private	288 (27.7)	27 (18.1)	315(26.5)
	Public	750 (72.1)	121 (81.2)	871(73.3)
Sex Male/Female (n=1,189)	Female	485 (46.6)	69 (46.3)	554(46.6)
	Male	555(53.4)	80 (53.7)	635(53.4)
Nutritional Status (n=1,123)	Severely Malnourished	153 (15.6)	39 (26.9)	192(17.1)
	Moderately Malnourished	314 (32.2)	59 (40.7)	373(33.2)
	Normal	425 (43.4)	41 (28.3)	466(41.5)
	Overweight	71 (7.2)	6 (4.1)	77(6.9)
	Obese	15 (1.5)	0 (0.0)	15(1.3)
Type of Pulmonary TB /Extra-Pulmonary TB (n=1,189)	PTB	828 (79.6)	122 (81.9)	950(79.9)
	EPTB	212 (20.4)	27 (18.1)	239(20.1)

In the diagnosis of tuberculosis among the TB-HIV co-infected patients, only 33.1% were bacteriologically confirmed while the rest were clinically diagnosed. Of the patients analyzed, the

patients who were smear positive at month zero are seen to have steadily converted to smear negative in the subsequent months following initiation of treatment. This is depicted in Figure 1.

Figure 1:

Sputum smear conversion of on TB-HIV co-infected patients in Kiambu County, Kenya, 2012-2016.



The age bracket 25-44 contributed the highest percentage of TB-HIV co-infected patients at 430/1,188 (36.3%). Similarly, the same age group had the highest mortality at 53/430 (36.2%). The ages (0-4)

and >55 years had the lowest number of cases at 21/1,188 (1.8%) and (77/1,188) 6.5% respectively as shown in figure 2.

Figure 2:

The distribution of TB-HIV co-infected patients and their treatment outcomes by age-groups in Kiambu County, Kenya, 2012-2016

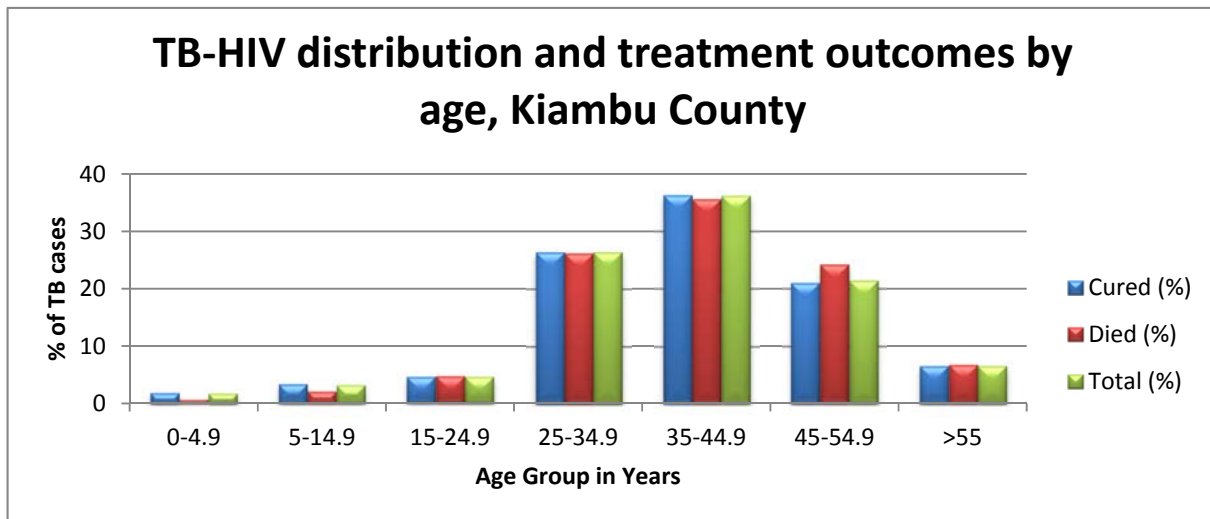
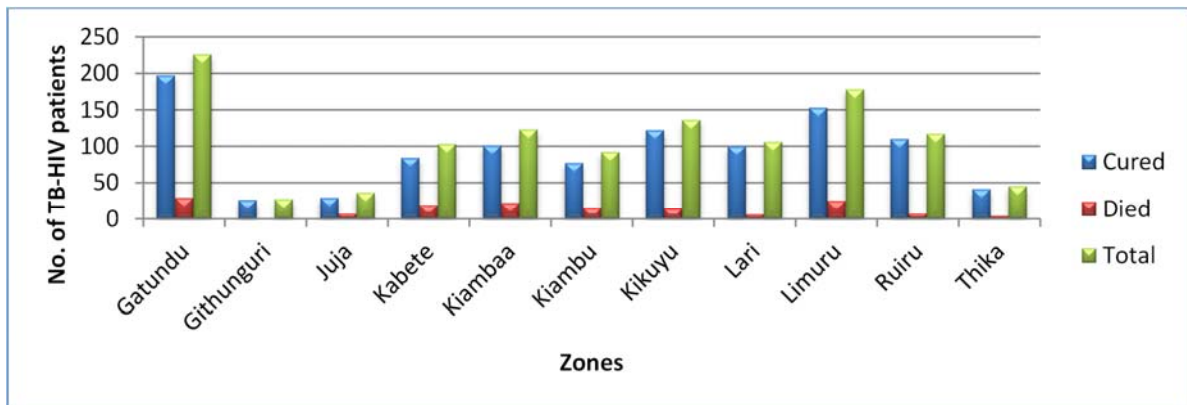


Figure 2: The distribution of TB-HIV co-infected patients and their treatment outcomes by age-groups in Kiambu County, Kenya, 2012-2016. Gatundu sub-county had the highest number of TB-HIV co-infected patients notified and also the

highest mortality prevalence, while Githunguri had the lowest TB and mortality prevalence. The other zones' prevalence is as shown in Figure 3 below.

Figure 3:

Distribution of TB-HIV co-infected patients, the cure rates and mortality rate by zone in Kiambu County, Kenya, 2012-2016.

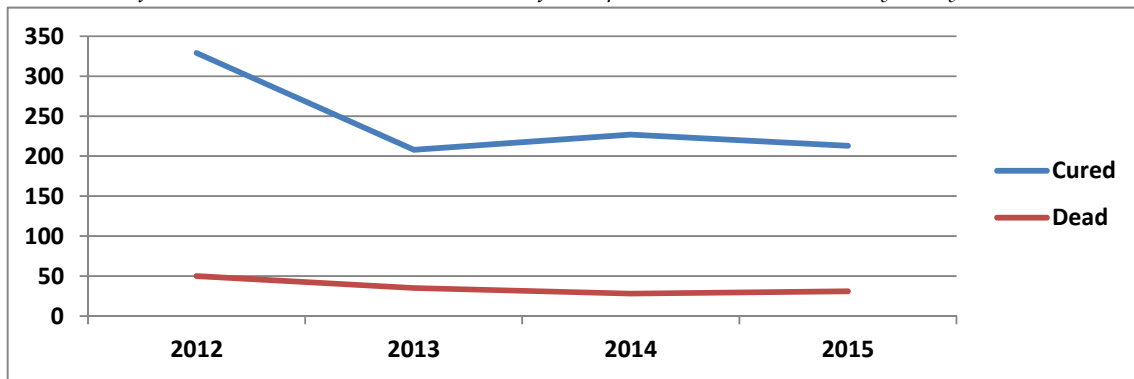


In the treatment outcome, there was a steady plateau from 2013 to 2015 with majority of the patients that were initiated on TB treatment were cured across the

years. The treatment outcomes for 2016 was not analyzed since most of the patients were still on treatment. This is shown in Figure 4.

Figure 4:

Trends of treatment outcomes in TB-HIV co-infected patients in Kiambu County, Kenya, 2012-2016

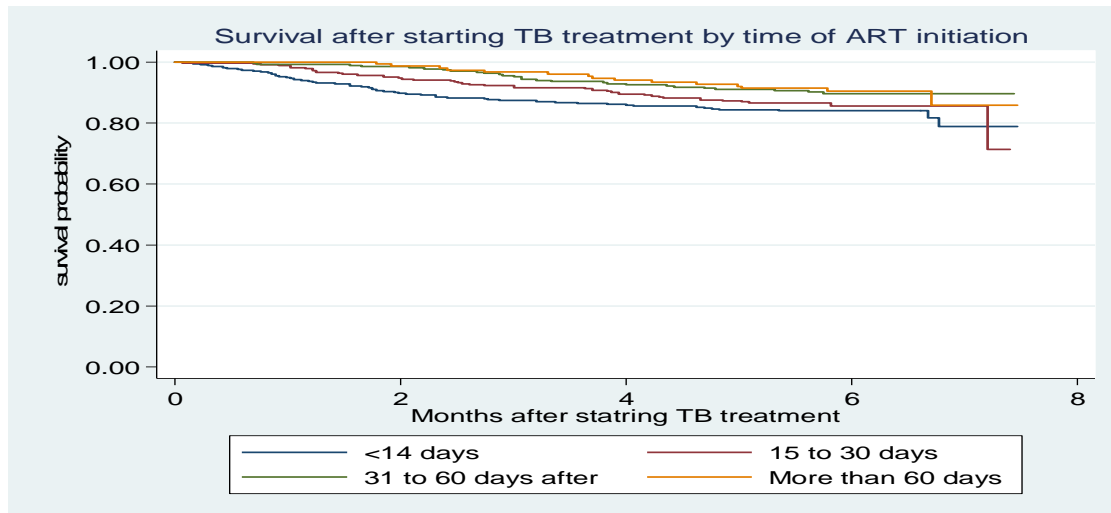


An eight month survival analysis based on the difference between the time of ART and TB medication initiation, shows a difference in survival of patients. Those started on ART treatment within 14 days of TB treatment initiation were less likely to

survive, when compared to those initiated on ART 15-30 days, then 31-60 days. The survival of the co-infected patients was best if the ART was initiated after 60 days as shown in figure 5.

Figure 5:

The survival after starting TB treatment by ART initiation in Kiambu County, Kenya 2012-2016



DISCUSSION

Majority of the TB-HIV co-infected patients presented with pulmonary tuberculosis. This could be due to the nature of tuberculosis transmission which is airborne, resulting to more of the disease being in the lung parenchyma. Studies done have shown that most patients typically present with pulmonary tuberculosis (PTB) and a lesser proportion presents with extra-pulmonary tuberculosis (EPTB) (12–15). TB notification was highest in the public sector which may be secondary to the existing support structures, for example, the sample transport referral networking as well as infrastructure in place for TB diagnosis. Further, most services in public sector are cost friendly to the patients. TB-HIV co-infection was prevalent among the productive age group 25-44. This is possibly attributable to the high prevalence of the twin disease in the County. Further, the age brackets affected are both sexually and economically active exposing them to a wide variety of risk factors of both tuberculosis and HIV infection. This is in line with the report done in 2015 by the national tuberculosis program

(16). Similarly, studies done in Northern Ethiopia showed that the age group most affected with TB-HIV co-infection was 25-45 years (17). The total number of the TB-HIV co-infected patients has been gradually declining over the years as supported by the national annual report (16). This could be due to the downward trend of the co-infected persons following successful TB-HIV interventions. In relation to the survival patterns, mortality was highest when the ART treatment was initiated before 14 days, followed by 15-30 days, then 31-60 days. The survival was best if the ART was initiated after 60 days. The peak in mortality within 0-14 days could possibly be due to the clinical deterioration from immune reconstitution inflammatory syndrome (IRIS), possible drug to drug interaction on anti-tuberculosis and anti-retroviral drugs, side effects that could result to halting some of the medication or pill burden which could greatly affect adherence. The findings are similar to studies done in Cambodia on early vs late ART initiation, which found that clients that were initiated on ART early had a higher mortality compared to those who had a late ART initiation (18).

In addition, studies done in South Africa on incidence, risk factors and impact on ART treatment initiation in TB-HIV co-infected patients revealed that the risk of developing IRD reduced when ART was initiated later during tuberculosis treatment. For instance, the risk of developing IRD was 100% when ART was initiated between 0-30 days and the risk markedly reduced to 7% when ART was initiated between 91-120 days(19). Similarly, a systemic review and metaanalysis conducted in 40 studies found an incidence of IRIS in 18% in TB-HIV co-infected patients upon ART initiation (20). Observational studies conducted in South Africa also found out that development of neurological disorders was notably high particularly in tuberculoma patients who were initiated on ART (21). This study has the advantage of having used the entire population of the newly diagnosed TB-HIV co-infected patients therefore eliminating the bias of small sample size. In addition, the data analyzed was precise and consistent based on the nature of data collection which means minimized errors. We also adhered to the STROBE guidelines. Further, it is the first study in Kiambu County that looked at the survival patterns of TB-HIV co-infected patients. However, some key variables like CD4 count was incomplete and viral load was not captured yet it could have had an influence on the survival patterns. The survival patterns were lower in the first 14 days and improved from 15 days onwards after ART initiation. There is need to strike an ideal balance between the risks and benefits of the client based on the clinical manifestations and diagnostic outcomes in order to commence treatment when the patient can fully tolerate both treatments with an aim of not only curing tuberculosis but also ensuring that the immune system of the client is being reconstituted. There is need to improve on CD4 count documentation in Kiambu County. There is need for a study that will monitor TB-HIV co-infected patients in the first 14 days following ART treatment initiation through both clinical and laboratory investigations.

CONCLUSION

In Kiambu County, the age group most prevalent for TB-HIV co-infection is 25-44 years. Nevertheless, interventions have been put in place that has seen the co-infectivity rate decline over the years. Following TB treatment commencement, the survival of the TB-HIV co-infected patients was highest if the ART treatment was initiated after the first two weeks onwards.

CONFLICT OF INTEREST: None

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