Does being on TB treatment predict a higher burden of problems and concerns among HIV outpatients in Kenya? A cross-sectional self-report study

Tuberculosis illness is associated with uncertain outcomes, and has high prevalence among people living with HIV. The new World Health Organization's End TB strategy specifies person-centred symptom management and psychosocial support alongside treatment within its pillars and components. There is a paucity of research to inform an effective care response in Kenya in terms of self-reported outcomes. We aimed to measure the three day period intensity of problems and concerns (physical, psychological, social and spiritual), and identify predictors of problems and concerns, among HIV patients attending outpatient care.

We conducted a cross-sectional self-report quantitative study among adult (aged at least 18 years) patients with confirmed HIV diagnosis, and aware of their diagnosis and attending HIV outpatient care in Kenya. Multi-dimensional palliative care problems and concerns were collected using African Palliative Outcome Scale (APOS). Ordinal logistic regression assessed the association of multi-dimensional problems and concerns controlling for demographic variables (age, gender, education and wealth) and clinical variables (WHO clinical stage, HIV treatment status, TB treatment status, and CD4 count).

We recruited N=400 participants. N=61 (15.64%) were on TB treatment. The items with worst score responses were help and advice to plan for the future (52.5%), ability to share feelings (46.25%), at peace (30.75%) pain (27%) and life worthwhile (18.75%). TB treatment status was associated with lower (worse) score for APOS total score (odds ratio .59, 95% CI .36 to .99; P=0.046) and factor 3(existential and spiritual wellbeing: .55, .32 to .92; p=0.023). Interestingly higher CD4 count was predictive of lower (worse) factor 3 outcomes (existential and spiritual wellbeing: .84, 95% CI 73 to .97; p=0.014).

This study informs the new WHO End TB policy with novel data on specific clinical needs. This calls for holistic symptom assessment, person-centred care and holistic management to respond positively to the End TB strategy.

Introduction

Kenya has the fourth largest HIV epidemic with 1.6 million people living with HIV (PLWH) (UNAIDS, 2016). Kenya also has highest prevalence of TB. Current data shows that there are 558 TB cases per 100,000 people (Voice of Africa, 2017).

Having HIV increases the likelihood of developing active pulmonary TB by 20 to 30 times (WHO, 2017). One third of HIV positive people in 2015 were infected with TB in Kenya. WHO global report suggested that Kenya is the one of the high burden TB countries (WHO, 2016). It is on top 20 on the lists of: (1) highest estimated number of incident TB cases >10,000 per year, (2) highest estimated numbers of incident TB cases among PLWH >1000 per year, and (3) highest estimated numbers of incident MDR-TB cases >1000 per year (WHO, 2015b). Approximately 30% of TB cases in Kenya are HIV positive (UNAIDS, 2016). TB is the fourth leading cause of death in Kenya (WHO, 2017). WHO estimated that in 2015, 35% of the deaths in HIV were related to TB (WHO, 2017).

UNAIDS sustainable development goal calls for the end of the global TB epidemic by 2030 including 90% reduction in TB deaths and 80% reduction in TB incidence rate. In order to achieve these goals the strategy proposes integration of TB and palliative care services. The new WHO End TB strategy calls for palliative care to attain zero suffering and advocates for access palliative care at each stage of the illness (WHO, 2015a). We aimed to measure problems and concerns among HIV patients attending outpatient clinic. The objectives were: (1) measure the three day period intensity of problems and concerns (physical, psychological, social and spiritual), and (2) identify predictors of problems.

Methods

Study design and participants

We did a cross-sectional study using self-report and file extraction among HIV/AIDS participants attending outpatient clinic at BOMU community hospital in Mombasa, Kenya. Adults (aged at least 18 years) with confirmed HIV diagnosis, and aware of their

diagnosis were included. We excluded those with significant physical or psychological impairment such that they were unable to give self-report data. Ethical approval was obtained from Kenyan Medical Research Institute (KEMRI/RES/7/3/1).

Data collection

We extracted CD4, treatment status for HIV and TB from patient's records. The other data was self-report and was collected in a private space at the clinic. All responses were recorded and answers given verbally by participants. This helped to reduce any potential response bias by mixing self-completion and research-completion. Data were collected using tools previously implemented/validated in African in HIV populations. The tools were:

1. Demographics, socioeconomic status using Demographic and Health Survey (DHS) (Gwatkin et al., 2007) and has previously been used in HIV research in sub-Saharan Africa (Lowther et al., 2012).

2. The African Palliative care Outcome Scale (APOS) was used to measure 3 day period of symptoms and concerns. It consists of seven items, scored on a 6-point (0-5) Likert scale. Possible scores range from 0-35 (with some items reversed), higher scores indicating the most positive outcomes (Harding et al., 2010). APOS had three validated subscales: (1) Physical and psychological wellbeing subscale (2) Interpersonal well-being subscale and (3) Existential well-being subscale (Harding et al., 2013).

Sample size calculation

Sample size calculation was based on HIV prevalence in Kenya. UNAIDS data report that 1.5 million Kenyans are infected with HIV (95% CI 1.3m, 1.6m) (WHO/UNAIDS, 2015). With 95% confidence, 5% margin of error, and a response distribution of 50% for any outcome we estimated that 385 were required to determine prevalence of any outcome (physical/ psychological symptom). We therefore recruited 400 to allow for any non-completers.

Data analysis

Data was entered into a spreadsheet with a unique identifier for each patient. The spreadsheet was converted into Stata version 14 dataset (StataCorp, 2015).

Descriptive statistics were used to profile the demographic, socioeconomic and clinical characteristics of participants. APOS scores were tabulated. All APOS subscales were computed and calculated based on the methods of APOS factor rather than just using APOS total scores which could potentially mask differences between domains. Because APOS total scores and factors 1, 2 and 3 were not normally distributed, they were converted into textiles. WHO clinical stages were combined (I and II combined to one group, likewise III and IV, because of small numbers).

Initial steps involved conducting a series of univariate analysis (ordered logistic regression) for demographic and clinical variables. The second step involved conducting multivariate analysis adjusting for demographic variables falling within less than 25% p value (Altman, 1991). All clinical variables were forced into the model regardless on the outcome of the univariate analysis because they important disease biomarkers which define HIV/AIDS state. We conducted a 'brant' test of parallel regression assumption. A non-significant test statistic provided evidence that the parallel regression assumption were met. All cases with missing data were excluded from the analysis.

Results

Sample characteristics and treatment variables

Table 1 presents the demographic characteristics and treatment variables of the participants. Of the 475 participants approached, 400 (84.2%) participated. The sample mean age was 39.4 years (SD 9.9).

Most of the patients were currently on ART (n=366, 91.5%), with (n=61, 15.64%) concurrent TB treatment. The mean CD4 count was 393.7(SD=238.2) range 2-1470. Most of the participants were at stage III/IV of HIV infection (n=348, 87%).

Table 1: Demographic and clinical characteristics (N=400)

Demographic characteristics	
Mean age (SD)	39.4 (9.9)
Female gender	280 (70%)
Education	
Primary	258 (64.5%)
Secondary	113 (28.25%)
Tertiary	29 (7.25%)
Wealth quintile	
Poorest	101 (25.25%)
Middle poor	59 (14.75%)
Middle	80 (20%)
Middle wealthy	80 (20%)
Wealthiest	80 (20%)
Clinical characteristics	
Physical performance (KPF)	
Mean(SD)	89.95 (13.53)
Range	40-100
CD_4 count	
Mean(SD)	393.7 (238.2)
Range	2-1470
WHO Stage	
Stage 1 and 2	52 (13%)
Stage 3 and 4	348 (87%)
Patient on ART	
Yes	366 (91.5%)
No	34 (8.5%)
Patient on TB treatment[1]	
Yes	61 (15.64%)
No	329 (84.36%)
Behavioural characteristics	
Told someone HIV Status	373 (93.25%)
Missed ART doses in the past 7 days[2]	
Yes	64 (16%)
No	302 (75.5%)
Mean(SD)	0.36 (1.28)
Range (number of missed doses)	1-14
APOS total scores, mean(SD) (0-35)[3]	21.45 (7.46)
APOS factor 1: Physical and psychological well-being, mean(SD) (0-15)[3]	10.66 (4.42)
APOS factor 2: Interpersonal well-being, mean(SD) (0-10)[3]	4.11 (3.18)
APOS factor 3: Existential and spiritual well-being, mean(SD) (0-10)[3]	6.68 (3.51)

Table 2: APOS (problems and concerns) reporting previous 3 days (n=400)

POS Item	0(worst status)	1	2	3	4	5 (Best status)	Mean(SD)
Pain	51 (12.75%)	57 (14.25%)	39(9.75%)	51(12.75%)	37(9.25%)	165(41.25%)	3.15(1.88)
Symptoms	27 (6.75%)	35 (8.75%)	37(9.25%)	54(13.5%)	47(11.75%)	200(50%)	3.65(1.66)
Worry	45 (11.25%)	16 (4%)	23(5.75%)	38(9.5%)	24(6%)	254(63.5%)	3.86(1.76)
Share feelings	159 (39.75%)	26 (6.5%)	32(8%)	37(9.25%)	22(5.5%)	124(31%)	2.27(2.17)
Life worthwhile	63 (15.75%)	12 (3%)	19(4.75%)	32(8%)	44(11%)	230(57.5%)	3.68(1.88)
Peace	93 (23.25%)	30 (7.5%)	24 (6%)	50(12.5%)	43(10.75%)	160(40%)	3(2.04)
Help and advise	193 (48.25%)	17(4.25%)	27(6.75%)	46(11.5%)	59(14.75%)	58(14.5%)	1.84(1.99)

[1] 10 missing

[2] 34 not on ART

[3] APOS: African Palliative Outcomes Scale, high scores better status

Predictors of problems and concerns

Following univariate analysis (table 3), multivariate models were constructed (table 4). TB treatment was associated with worse symptoms and concerns (APOS total score: odds ratio (OR) .59, 95% CI .36 to .99; P=0.046) and factor 3 (existential and spiritual wellbeing: .55, 95% CI .32 to .92; p=0.023). Interestingly a higher CD4 count was predictive of lower (worse) scores for factor 3 (existential and spiritual wellbeing: OR .84, 95% CI 73 to .97; p=0.014).

Age was predictive of higher (better) scores for palliative care symptoms and concerns (APOS total scores: OR 1.03; p= 0.005), factor 2 (interpersonal wellbeing: OR 1.03; p=0.004), and factor 3 (existential and spiritual wellbeing: OR 1.03; p=0.001).

Female gender was predictive of lower (worse) scores for factor 1 (physical and psychological wellbeing: OR .59; p=0.013).

Table 3: Univariate association of socio-demographic and clinical variables with POS total score and POS factors as dependent variables (n=390)

Independent variables	**Outcomes (dependent variables**			
	APOS total	Factor 1: (physical and psychological)	Factor 2: interpersonal well-being	Factor 3: existential and spiritual
	OR (95% CI) p value	OR (95% CI) p value	OR (95% CI) p value	OR (95% CI) p value
Age	1.03 (1.02 to 1.05) 0.002*	1.01 (.99 to 1.03) 0.28	1.03 (1.01 to 1.05) 0.003*	1.03 (1.01 to 1.05) 0.001*
Gender (ref female)	.68 (.46 to 1.01) 0.059*	.57 (.38 to .85) 0.006*	1.28 (.86 to 1.91) 0.23*	.75 (.50 to 1.13) 0.17*
Clinical stage (stage 1/2 vs stage 3/4)	.79 (.46 to 1.36) 0.40	1.30 (.76 to 2.22) 0.96	.75 (.44 to 1.25) 0.27	1.16 (.68 to 1.98) 0.59
ART (ref yes)	1.49 (.77 to 2.87) 0.23*	1.76 (.92 to 3.37) 0.086*	1.37 (.71 to 2.63) 0.35	1.37 (.72 to 2.62) 0.34
CD4 count	.93 (.83 to 1.05) 0.25*	.98 (.87 to 1.11) 0.78	.96 (.84 to 1.09) 0.51	.88 (.78 to 1.01) 0.072*
TB treatment (ref yes)	.57 (.35 to .95) 0.029*	.62 (.37 to 1.02) 0.059*	.92 (.56 to 1.54) 0.77	.56 (.34 to .94) 0.027*
Education: Primary vs Secondary	1.13 (.76 to 1.70) 0.54	1.18 (.78 to 1.78) 0.43	1.36 (.91 to 2.04) 0.14*	.72 (.47 to 1.08) 0.12*
Primary vs Tertiary	1.64 (.81 to 3.31) 0.17*	1.24 (.64 to 2.41) 0.53	1.49 (.75 to 2.97) 0.26	1.04 (.50 to 2.16) 0.91
Wealth: Poorest vs middle poor	1.77 (.98 to 3.19) 0.056	1.95 (1.09 to 3.51) 0.025*	1.59 (.87 to 2.88) 0.13	1.29 (.70 to 2.35) 0.41
Poorest vs middle	1.42 (.82 to 2.25) 0.21*	1.73 (1.01 to 2.97) 0.046*	1.06 (.61 to 1.82) 0.84	1.19 (.69 to 2.06) 0.53
Poorest vs middle wealthy	1.60 (.92 to 2.76) 0.095*	1.37 (.80 to 2.36) 0.25*	1.85 (1.09 to 3.15) 0.023*	1.14 (.66 to 1.94) 0.64
Poorest vs wealthiest	.93 (.54 to 1.59) 0.78	1.29 (.74 to 2.22) 0.37	1.57 (.91 to 2.70) 0.11*	.67 (.39 to 1.17) 0.16*

POS: African Palliative Outcome Scale; CI: confidence interval

*Significant at the 25% level and subsequently entered into the multivariable model

Table 4: Multivariate analyses for total POS scores and POS factors as dependent variables (n=390)

Independent variables	**Outcomes (dependent variables**			
	APOS total	Factor 1: (physical and psychological)	Factor 2: interpersonal well-being	Factor 3: existential and spiritual
	OR (95% CI) p value	OR (95% CI) p value	OR (95% CI) p value	OR (95% CI) p value
Age	1.03 (1.01 to 1.05) 0.005*	-	1.03 (1.01 to 1.05) 0.004*	1.03 (1.01 to 1.06) 0.001**
Gender (ref female)	.69 (.47 to 1.05) 0.081	.59 (.39 to .89) 0.013*	1.41 (.93 to 2.14) 0.11	.72 (.47 to 1.11) 0.14
Clinical stage (stage 1/2 vs stage 3/4)	.79 (45 to 1.38) 0.41	1.17 (.67 to 2.05) 0.57	.84 (.49 to 1.43) 0.51	1.22 (.69 to 2.13) 0.50
ART (ref yes)	1.30 (.66 to 2.56) 0.44	1.63 (.84 to 3.17) 0.15	1.10 (.56 to 2.16) 0.78	1.16 (.59 to 2.27) 0.67
CD4 count	.91 (.80 to 1.04) 0.16	.98 (.86 to 1.11) 0.72	.94 (.82 to 1.07) 0.36	.84 (.73 to .97) 0.014*
TB treatment (ref yes)	.59 (.36 to .99) 0.046*	.61 (.37 to 1.02) 0.059	.97 (.57 to 1.63) 0.90	.55 (.32 to .92) 0.023*
Education: Primary vs Secondary	1.01 (.65 to 1.54) 0.98	-	1.26 (.82 to 1.93) 0.29	.67 (.43 to 1.04) 0.071
Primary vs Tertiary	1.78 (.84 to 3.76) 0.13	-	1.37 (.66 to 2.85) 0.40	1.22 (.56 to 2.68) 0.62
Wealth: Poorest vs middle poor	1.70 (.93 to 3.10) 0.083	1.77 (.97 to 3.22) 0.061	1.59 (.86 to 2.92) 0.14	1.26 (.67 to 2.35) 0.47
Poorest vs middle	1.24 (.71 to 2.17) 0.45	1.69 (.97 to 2.92) 0.062	.97 (.56 to 1.70) 0.93	1.05 (.60 to 1.86) 0.86
Poorest vs middle wealthy	1.36 (.77 to 2.42) 0.29	1.32 (.75 to 2.30) 0.33	1.74 (1.00 to 3.04) 0.051	1.02 (.58 to 1.82) 0.94
Poorest vs wealthiest	.74 (.41 to 1.34) 0.32	1.15 (.66 to 2.02) 0.63	1.35 (.75 to 2.41) 0.32	.60 (.33 to 1.11) 0.11
Tests of parallel regression assumption	Brant test =5.99 p=0.92	Brant test =9.81 p=0.37	Brant test =16.62 p=0.17	Brant test =15.5 p=0.22

APOS: African Palliative Care Scale; CI: Confidence interval; TB: Tuberculosis

Significant at *5% level, **1% level

Discussion

Our study presents novel data on problems and concerns among HIV patients attending outpatient clinic in Kenya. Sample size was larger in our study compared to other studies conducted in sub-Saharan region (Harding, Defilippi, & Cameron, 2016). Recruitment rate was highly successful (84.2%). However this was a cross-sectional study, therefore we can only identify associations, not causality. We excluded participants who were unable to complete questionnaires with assistance from our data collector, therefore this data may underestimate the prevalence and burden of the multidimensional problems and concerns.

The significant existential and spiritual wellbeing experienced by patients on TB treatment confirms the need for personal-centred care for patients (Harding et al., 2016). WHO recommends palliative care approach among patients on TB treatment (WHO, 2017)**.** Existing professionals providing palliative care for HIV, cancer can translate directly into TB. The significant worsening in existential and spiritual wellbeing scores by patients with high CD4 counts confirms that clinically the patient may be better but may have spiritual problems. ART can only improve the immune system/increase the CD4 count, but the spiritual needs still persist. This calls for holistic management for patients even though they may have a strong immune system. A cross-sectional study among HIV (81%) and cancer (18%) conducted in Uganda and South Africa reported 27% burden of worst peace scores (Selman, Harding, Higginson, Gysels, & Speck, 2011).

Palliative care services are needed among patients with HIV and TB to improve quality of life through integration of HIV and TB care and providing holistic and individualised care, through reducing stigma associated with TB treatment, and compassionate care (Hospice Palliative Care Association of South Africa, 2011). The provision of TB care focussing solely on technical aspects of care is not enough to meet the needs of patients on TB treatment (Harding et al., 2005). Palliative care helps to control symptoms associated with TB and comorbidities such as neuropathy due to side effects of Isoniazid (Breen, Lipman, & Johnson, 2000). Palliative care approach will help to improve patient's well-being and

promote drug adherence. Poor drug adherence in TB leads to development of MDR-TB which is more costly and requires highly toxic drugs (Harding et al., 2016).

A systematic review reported that HIV palliative care for chronic illnesses including TB improves problems and concerns (Harding et al., 2005). Previous evidence among cancer and HIV patients including their families show that palliative care services improves outcomes (Higginson & Evans, 2010). We therefore recommend integration of palliative care for TB alongside existing services such as HIV. Our novel data informs clinical practice to implement guidelines for providing palliative care to patients with TB and the new WHO End TB strategy (Hospice Palliative Care Association of South Africa, 2011; WHO, 2015a). All health workers must receive training in palliative care to equip them with skills to undertake routine assessments of patients with TB such as pain and symptom and provide appropriate interventions and support for their problems.

References

Altman, D. G. (1991). *Practical statistics for medical research*. London: Chapman and Hall.

Breen, R. A., Lipman, M. C., & Johnson, M. A. (2000). Increased incidence of peripheral neuropathy with co-administration of stavudine and isoniazid in HIV-infected individuals. *AIDS, 14*(5), 615.

Gwatkin, D. R., Rutstein, S., Johnson, K., Suliman, E., Wagstaff, A., & Amouzou, A. (2007). *Socio-Economic Differences in Health, Nutrition, and Population*. Retrieved from Ghana:

Harding, R., Defilippi, K., & Cameron, D. (2016). What palliative care–related problems do patients with drug-resistant or drug-susceptible tuberculosis experience on admission to hospital? A cross-sectional self-report study. *Palliative Medicine, 30*(9), 862-868. doi:10.1177/0269216316637240

Harding, R., Karus, D., Easterbrook, P., Raveis, V. H., Higginson, I. J., & Marconi, K. (2005). Does palliative care improve outcomes for patients with HIV/AIDS? A systematic review of the evidence. *Sex Transm Infect, 81*. doi:10.1136/sti.2004.010132

Harding, R., Selman, L., Agupio, G., Dinat, N., Downing, J., & Gwyther, L. (2010). Validation of a core outcome measure for palliative care in Africa: the APCA African palliative outcome scale. *Health Qual Life Outcomes, 8*. doi:10.1186/1477-7525-8-10

Harding, R., Selman, L., Simms, V. M., Penfold, S., Agupio, G., Dinat, N., . . . Siegert, R. J. (2013). How to Analyze Palliative Care Outcome Data for Patients in Sub-Saharan Africa: An International, Multicenter, Factor Analytic Examination of the APCA African POS. *Journal of Pain and Symptom Management, 45*(4), 746-752. doi:http://dx.doi.org/10.1016/j.jpainsymman.2012.04.007

Higginson, I., & Evans, C. (2010). What is the evidence that palliative care teams improve outcomes for cancer patients and their families? *Cancer J, 16*, 423 - 435.

Hospice Palliative Care Association of South Africa. (2011). Guidelines for providing palliative care to patients with tuberculosis South Africa: Pinelands.

Lowther, K., Simms, V., Selman, L., Sherr, L., Gwyther, L., Kariuki, H., . . . Harding, R. (2012). Treatment outcomes in palliative care: the TOPCare study. A mixed methods phase III randomised controlled trial to assess the effectiveness of a nurse-led palliative care intervention for HIV positive patients on antiretroviral therapy. *BMC Infect Dis, 12*, 288. doi:10.1186/1471-2334-12-288

Selman, L., Harding, R., Higginson, I. J., Gysels, M., & Speck, P. (2011). Spiritual wellbeing in sub-Saharan Africa: the meaning and prevalence of 'feeling at peace'. *BMJ Supportive & Palliative Care, 1*(Suppl 1), A22-A22. doi:10.1136/bmjspcare-2011-000020.66

StataCorp. (2015). Stata Statistical Software (Version Release 14). College Station, TX: StataCorp LP.

UNAIDS. (2016). *Prevention Gap Report*. Retrieved from http://www.unaids.org/sites/default/files/media_asset/2016-prevention-gap-report_en.pdf

Voice of Africa (Producer). (2017, 14/06/2017). Kenya Releases Results of National TB Prevalence Survey. Retrieved from https://www.voanews.com/a/kenya-releases-results-national-tb-prevalence-survey/3780722.html

WHO. (2015a). The End TB Strategy: Global Strategy and Targets for Tuberculosis Prevention, Care and Control after 2015. Retrieved from http://www.who.int/tb/post2015_TBstrategy.pdf?ua=1

WHO. (2015b). Use of high burden country lists for TB by WHO in the post-2015 era Retrieved from http://www.who.int/tb/publications/global_report/high_tb_burdencountrylists2016-2020.pdf

WHO. (2016). Global Tuberculosis report. Retrieved from http://www.who.int/tb/publications/global_report/gtbr2016_annex2.pdf?ua=1

WHO. (2017). Tuberculosis. *Fact Sheet.* Retrieved from http://www.who.int/mediacentre/factsheets/fs104/en/

WHO/UNAIDS. (2015). Global AIDS Response Progress Reporting 2015. Retrieved from http://www.unaids.org/sites/default/files/media_asset/JC2702_GARPR2015guidelines_en.pdf