Cascade Variabilities in TB Case Finding among People Living with HIV and the Use of IPT: Assessment in Three Levels of Care in Cross River State, Nigeria

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Authors' contributions

This work was carried out in collaboration among all authors. Author MO designed the study, performed the statistical analysis, wrote the protocol and wrote the first draft of the manuscript. Authors KCO and EIO managed the analyses of the study. Authors AB, EUE, MI, JOB and AOP managed the literature searches. All authors read and approved the final manuscript.

Original Research Article

ABSTRACT

TB is the most common cause of morbidity and mortality in people living with HIV/AIDS (PLHIV) as it accelerates the progression of HIV infection. Every PLHIV is at an annual risk of 10% and a lifetime risk of 50% to acquiring TB and TB is responsible for the death of 30-40% PLHIV. We undertook to assess the WHO recommended intensified TB case finding among PLHIVs in three of levels of ART clinics in cross River State, Nigeria. We used quantitative method to review retrospectively collected routine TB and HIV facility data from University of Calabar Teaching

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hospital, Calabar; Infectious disease Hospital, Calabar and primary Health Centre, Calabar Municipal ART clinics. The study population for intensified case finding and IPT comprised of available records of HIV- positive patients ≥15 years old seen at the selected facilities for clinical care and treatment from January to December 2016 and January to December 2018. A cohort sampling strategy was used to assess the ICF cascade and IPT uptake. Data collection lasted from 15th to 31st November 2019 in the first phase and had extension to February 2020 due to delayed ethical clearance from the University of Calabar Teaching hospital. Quantitative data was analysed using Stata 13.0 to produce descriptive statistics including frequencies and percentages for categorical variables. Of the 326 PLHIVs (115 females) in the records, 311 had their TB screening recorded (95%). 155(50%) were screen positive while 326(210%) were evaluated for TB in the lab, out of which 182 (56%) were TB confirmed. PLHIVs ages 25-29 years were most affected, with more persons being evaluated for TB before the `test and treat` policy. Of the 207 PLHIVs started on IPT, 103 (99%) started before `test and treat` compared to 102(91%) after policy. IPT uptake was highest among ages 25-29 years. This evaluation shows that intensified case finding among PLHIV is feasible and has a high prospect for TB case finding among PLHIVs. However, critical gaps exist- poor documentation and linkages on the clinical and diagnostic arm of the cascade makes it impossible to estimate yield in a cohort and present the situation of weak clinical interphase with people seeking care.

1. INTRODUCTION

The negative impact of TB and HIV makes them the two most important infectious diseases across the globe. Countries with a high burden of the disease are frequently left with a trail of socio-economic vulnerabilities at family and community levels. In 2016, more than 1 million people died from TB and nearly 2 million people were infected with HIV [1]. The huge burden of poverty and comparatively low literacy levels in sub-Saharan Africa creates a perfect storm for the sustained propagation of these diseases. Poor TB case finding remains a global concern [2]. Even though TB is curable, treatment is only possible when the infected persons are diagnosed and started on anti-TB drugs. TB case finding among PLHIV is crucial to reducing the morbidity and mortality of the disease among co-infected patients: Diagnosed TB cases can be treated and persons without signs of TB can be placed on isoniazid preventive therapy to significantly minimize the risk of acquiring the disease [3]. The challenges of poor TB case finding are a result of both health systems weakness in the human resource and infrastructure architecture of individual countries. Implementation of the WHO recommended 3 `i`s for reducing the burden of TB among PLHIVs, that is, intensified TB case finding among PLHIV, isoniazid preventive therapy for uninfected PLHIVs and TB infection control in health care and congregate settings, is often in letters than practice, hence the overall negative influence of both infections continues to ravage the world despite huge global investments and board room conversations.

Nigeria is a high HIV and TB burdened country with an average TB prevalence of 27% among HIV-positive persons and TB incidence of 219 per 100,000 population [4,5]. Nigeria has an HIV prevalence of 1.4% among the general population, with 18 deaths per 100,000 among populations co-infected with the disease (Nigeria AIDS Indicator Survey, 2018). TB case notification has remained sub optimal in the country despite several efforts by national government and donor partners. In 2017, Nigeria reported only 104, 904 cases among her population of almost 200 million people [5]. Several reasons are responsible for the poor TB detection and notification; many of them are site and region specific, with significant variability across the geopolitical regions of the country. Even though protocols, guidelines, job aids and monitoring tools may be in place, the fidelity in implementation is uncertain in most parts of the country. No doubt, there are community and health system factors that influence the transmission and reduction of infectious diseases- we seek to investigate the issues that are within the health system. What are the gaps in the clinical and programmatic management of TB & HIV co-infection in Nigeria within the health system? This study sought to identify these gaps, with focus on the three (3) levels of the health system in 3-selected facilities in Cross River State, Nigeria. Cross River is one of the states in the south-south geo-political region of Nigeria,

with a population of about 3.5 million people. The state had a TB smear positivity of 2.4% in 2008 and 24.4% in 2012 with 795 and 1781 TB cases notified respectively [6]. This study will describe missed opportunities and provide understanding on the status quo at three levels of health services in Cross River State, Nigeria, for TB case finding among people living with HIV (PLHIV) with a reflection on the situation before and after the WHO policy of `test and treat`. We will also proffer approaches to addressing the observed gaps and share good policy recommendations and valuable information to improve practice in the care of PLHIVs and TB patients.

2. MATERIALS AND METHODS

2.1 Study Design

A quantitative method was used to retrospectively review routine TB and HIV facility data, including the TB screening and IPT uptake on the patient care cardin the anti-retroviral therapy clinics, referral logs and the lab testing records.

2.2 Study Setting

The study was conducted at the University of Calabar Teaching hospital, Calabar (UCTH); Infectious disease Hospital (IDH), Calabar and primary Health Centre, Calabar Municipal. UCTH

is the only tertiary health facility in the state, IDH is the main TB referral hospital in the area while PHC is one of the primary health facilities in municipal area. These facilities were selected to ensure representation of the three levels of health care in Cross River State, Nigeria.

2.3 Study Population and Sampling

The study population comprised of available records of HIV- positive patients ≥15 years old seen at the selected facilities for clinical care and treatment for HIV from January to December 2016, and January to December 2018. A cohort sampling strategy was used to assess the intensified case finding (ICF) cascade. Data collection lasted from 15th to 31st November 2019 in the first phase and had extension to February 2020 due to delayed ethical clearance from the University of Calabar Teaching hospital.
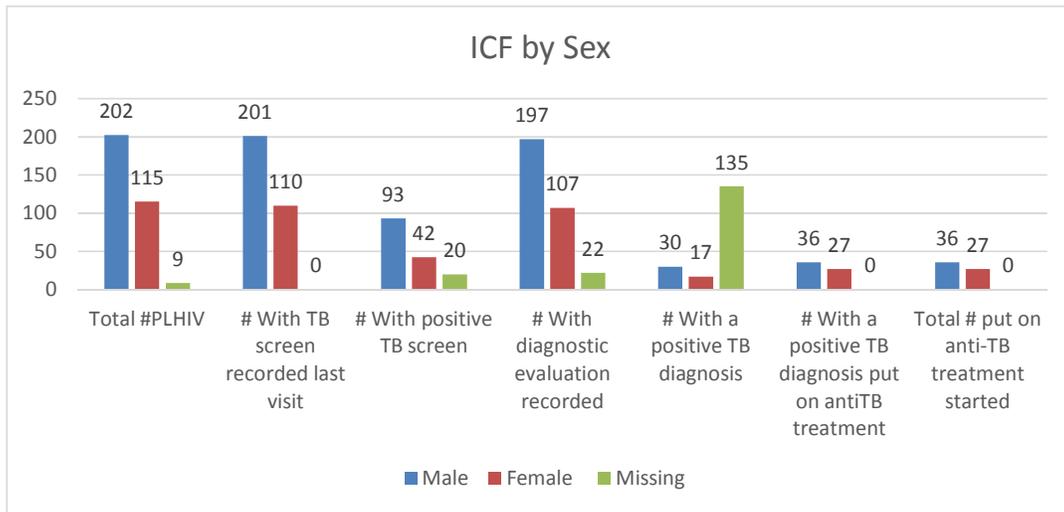
2.4 Data Management

Collected data was entered by trained data clerks and cleaned for missing or invalid values by the study coordinator. The data collection tool was restricted not to contain patient identifying information. Quantitative data was analysed using Stata 13.0 to produce descriptive statistics including frequencies and percentages for categorical variables. Relevant charts and colour diagram were developed to compare specific descriptive data.

3. RESULTS

**Table 1. Summary data-ICF cascade in HIV care and treatment settings**

Column1	Total #PLHIV	# With TB screen recorded last visit	# With positive TB screen	# With diagnostic evaluation recorded	# With a positive TB diagnosis	# With a positive TB diagnosis put on anti TB treatment	Total # put on anti-TB treatment started
Gender							
Male	202	201	93	197	30	36	36
Female	115	110	42	107	17	27	27
Missing	9	0	20	22	135	0	0
Age							
<25 years	24	24	9	22	4	7	7
25-29 years	244	238	106	234	37	48	48
50 years and above	49	49	20	48	6	8	8
Missing	9	0	20	22	135	0	0
ART start period							
After test and start	127	127	78	133	19	**16**	**16**

| Column1	Total #PLHIV	# With TB screen recorded last visit	# With positive TB screen	# With diagnostic evaluation recorded	# With a positive TB diagnosis	# With a positive TB diagnosis put on anti TB treatment	Total # put on anti-TB treatment started
Before test and start	176	177	57	171	28	**42**	**42**
Missing	9	7	20	**22**	135	**5**	**5**
Facility							
Primary	134	121	17	114	**0**	**17**	**17**
Tertiary	183	190	118	190	**47**	46	46
Missing	9	0	20	**22**	**135**	0	0

Fig. 1. Intensified case finding of TB among PLHIVs by sex

Reflection: Most of the patients available for evaluation were males. More PLHIV (326) were sent for TB diagnosis than the number with a positive TB screen (155). Many PLHIV TB status was missing.
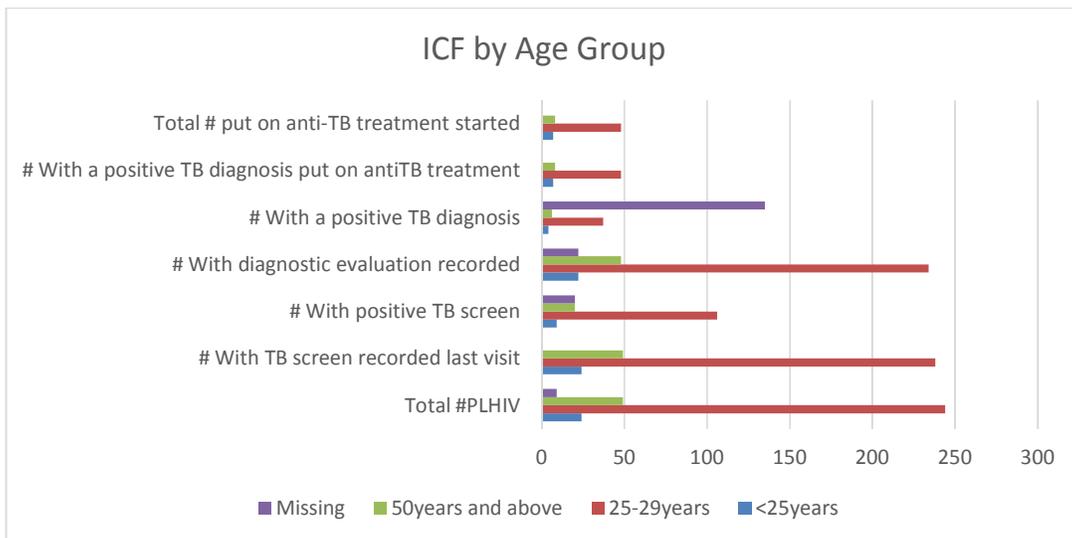
Fig. 2. Intensified case finding of TB among PLHIVs by age

Reflection: Available record show age group 25-29 yrs were consistently the most prevalent across the cascade. Again, many PLHIVs with a TB diagnosis had missing TB status.
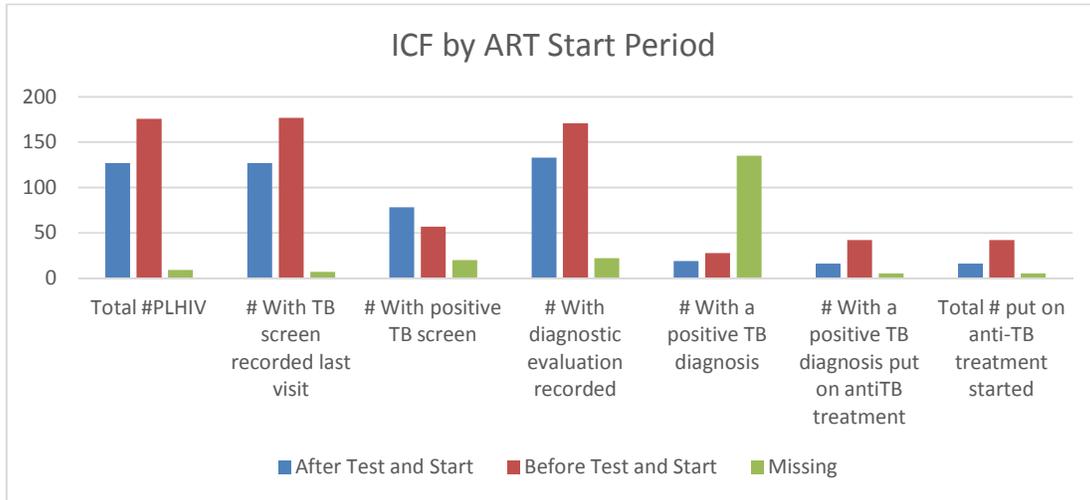
Fig. 3. Intensified case finding of TB among PLHIVs by ART start period

Reflection: TB screening, diagnosis and linkage to treatment was generally better before test and treat.

Table 2. Percentage of eligible PLHIV started IPT

	# IPT eligible (negative screen or diagnostic)	# IPT started (% of eligible per category/row)
Gender		
Male	138	132(95.7%)
Female	69	64(92.8%)
Total	207	196(94.7%)
Age		
<25years	12	12(100%)
25-29years	156	147(94.2%)
50years and above	39	37(94.9%)
Total	207	196(94.7%)
ART start period		
After Test and Start	103	102(99%)
Before Test and Start	102	93(91.2%)
Missing	4	1(25%)
Total	207	196(94.7%)
Facility		
Primary	64	55(85.9%)
Tertiary	143	141(98.6%)
Total	207	196(94.7%)

Reflection: Average of over 90% of eligible recipients of care across parameters documented were started on.
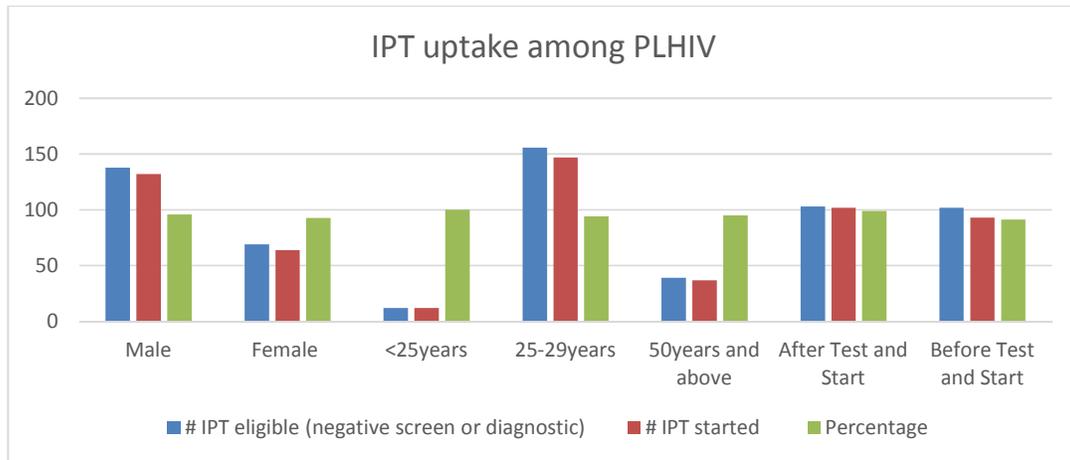
Fig. 4. IPT uptake among PLHIV screened for TB at the ART enrolment desk

Reflection: IPT uptake was better among ages 25-29 and after the `test and treat` policy

Table 3. Distribution of patient before and after test and start

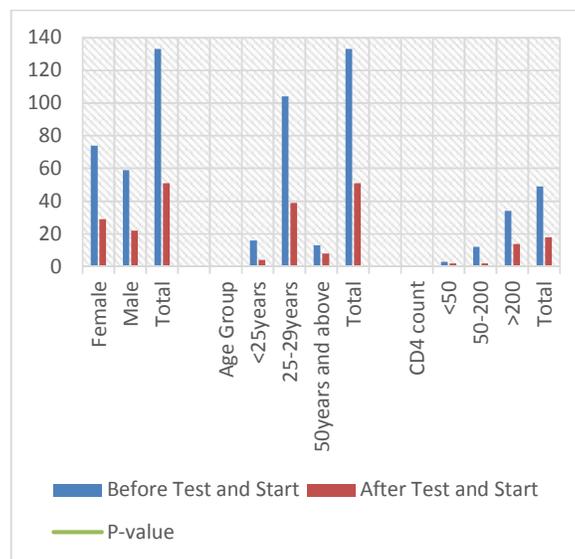| Gender	Before Test and Start	After Test and Start	P-value
Female	74	29	0.30
Male	59	22	
Total	133	51	
Age Group			
<25years	16	4	0.46
25-29years	104	39	
50years and above	13	8	
Total	133	51	
CD4 count			
<50	3	2	0.57
50-200	12	2	
>200	34	14	
Total	49	18	

Fig. 5. Distribution of patient before and after test and start

Reflection: Across all parameters, more TB patients accessed ART before the introduction of the WHO test and treat policy. Across all the CD4 levels in consideration, more TB patients accessed ART before `test and treat`. More of the TB patients who were started on ART did so at CD4 above 200.

4. DISCUSSION

TB intensified case finding and treatment among PLHIV is premised on three levels of cross-cutting program commitment: to establish and strengthen the mechanisms for delivering integrated TB and HIV services, reduce the burden of TB in people living with HIV and initiate early antiretroviral therapy to reduce the burden of HIV disease in persons who may be co-infected with presumptive and diagnosed TB. This study reviewed the routine data that supports TB and HIV integration at three levels of care in Cross River State, Nigeria, with the view to finding the gaps that exist in TB case finding among PLHIVs within the object of the WHO recommended integration, so as to inform recommendations to the national TB and leprosy control program (NTBLCP) and the Nigeria National Aids Control Program (NACA) for improvement planning.

Missing data due to poor documentation of clinical and laboratory events was a critical observation in the assessment study, and a major limitation in proposing valuable evidence to buttress or refute the hypothesis. The observation is however a true reflection of the situation of TB/HIV integration across the levels of care, and perhaps a measure of the quality of health care being offered to the affected population. Most of the quantitative data from the secondary facility for intensified case finding and HIV situation among TB patients were missing altogether and was therefore not included in the evaluation.

Most of the PLHIVs available on record for evaluation were men. This is not consistent with what is already known, that HIV generally affects more females than males [7] and also that more women than men present at the ART clinics due to better health seeking behaviour [8] albeit with fluctuation based on cultural and economic biases [9]. In this study, a lot more PLHIVs (210%) were sent to the TB diagnostic unit for definitive TB diagnosis than the number that received clinical screening. This is contrary to documentations in pilot programs in Sub-Saharan Africa where the true cascade is followed through, many of them showing far less presumptive TB patients reaching the diagnostic point than the number originally screened positive for TB [10]. Der et al. (2020) showed in a similar cascade analysis in rural and urban Ghana that most of the losses are due to the long travel distance between the service delivery points [11]. In this study, the huge positive difference could be traceable to referrals from other facilities, or a return of old PLHIVs who were referred for TB screening and got lost in transit, only to return later, or a mix of all these. In all, the weakness in tracking the referrals makes it difficult for the program to be able to keep an accurate tracker of the TB/HIV cascade events. The cascade has been used as a measure of quality of service in many settings as gaps along the cascade, when improved, will consequentially reflect in the quality of screening and diagnosis and ultimately in treatment outcomes [12].

Available record show age group 25-29 yrs were consistently the most prevalent across the cascade. This reflects the age bands most affected in TB and HIV diseases in Nigeria, and incidentally are also the most economically active age group of the economy, a reflection of the socio-economic impact of both diseases on the national life. Again, many PLHIVs with a TB diagnosis had missing TB status. It is possible that the missing TB status on the available record could be the result of the undocumented referral activity of PLHIVs with `any positive sign` on the TB screening clinical algorithm, sent to a diagnostic service delivery point (AFB, Xpert or X-ray) without a return to record the outcome; or it could be that patients are lost in transit, back home, or to another facility, or that records are not just entered upon return of the clients; may be a mix of all these factors. The huge gap between PLHIVs accessing the ICF and the number with a positive TB screen (50%) suggest the reasonable completeness of TB screening and the documentation at this level. In most ART facilities, TB screening is indicated on the ART care card, and it often indicates over 98% completeness. However, the fidelity of that documentation is a resonating question across national programs. Poor compliance with actual screening of TB among PLHIVs, plus huge losses of complete referrals from the clinic to the labs/x-ray units contributes to poor TB case detection. The observation in this study has been

collaborated in similar studies across Africa and may possibly contribute to the falling global incidence of TB, estimated at 1-2% per annum, a major risk to the end TB target by 2030 [13,14]. Out of 4160 symptomatic encounters in a similar study in Kenya, only 1.6% (66) and 7.45 (309) reached sputum microscopy and AFB respectively [15].

The TB screening, diagnosis and linkage to treatment was generally better before the ``test and treat`` policy. The objective of the WHO-recommended `test and treat` policy was to promote early enrolment of newly diagnosed PLHIVs into life-saving antiretroviral therapy, and thereby mitigating the development of advanced HIV disease [16] PLHIVs started early on ART are able to achieve viral suppression within 4-6 months acquire immune recovery and live long and normal lives [17]. However, implementation of the policy has had its fair share of negative impact on the care of PLHIVs, especially in the environment of the crowded clinics that characterise the ART clinics in most developing countries.

4.1 Isoniazid Preventive Therapy

Over 90% of eligible recipients of care across parameters documented were started on IPT. This is contrary to what is widely known. Since the introduction of IPT, coverage has remained very low across many countries, often due to drug stockout and poor health worker perception [18,19]. Pill burden, long duration of administration and toxicity has also been raised at various times as the downside of IPT [20]. The documentation observed here could well be the one done just for the limited persons that were eligible and that accepted to start IPT. Completion outcomes were also not documented; hence the outcome measures of IPT could not be evaluated. IPT administration should ideally measure outcomes: TB status, deaths and losses to follow up. It is not clear whether the policy had any programmatic value on the commencement and completion of IPT in the facilities assessed, but what is generally known is that the commencement of the `test and treat` policy in 2017, coincided with the period when there was a globally heightened call for IPT scale up. The importance of preventing TB among PLHIV makes the TB screening all very important, to quickly identify persons who are not presumptive, and to start them very early on TPT. This will also be an effective complement to protect the recipients of care attending the clinic

from the huge lapses in administrative end of infection control.

Across all parameters, more TB patients accessed ART before the introduction of the WHO test and treat policy. This is contrary to the observation on the HIV end of the cascade. Test and treat implied starting ART immediately after being tested positive to HIV. Ordinarily, the policy ought to have had a direct bearing on ART start time for TB patients. That means, more TB patients ought to have been started on ART after the initiation of the policy. This was not the case. One possible explanation could be that most of the TB patients in 2016 and prior, were being quickly started on ART because of their presentation, and it could be because after the policy, persons who were seen were less ill and the health workers wanted to observe their wellbeing on TB treatment before ART initiation. The national guidelines recommend, where necessary due to severe illness in the recipient of care, to delay ART by 2-weeks to minimize the effect of pill burden and side effects [21].

Across all the CD4 levels in consideration, more TB patients accessed ART before `test and treat`. More of the TB patients who were started on ART did so at CD4 above 200, indicating a reasonably better immune entry to care. Beyond the better prognostic value and positioning, TB, as one of the WHO clinical stage 3 criteria in HIV management and a known killer of PLHIVs, is an indication for immediate start of ART. However, Cure rates were better before the test and treat policy- an observation that was noted as very concerning. We don't know whether `test and treat` negatively impacted on co-administration of ART and TB treatment? Pill burden is a notable reason for poor adherence, in addition to lack of food, poor communication between patients and health workers, traditional alternative medicine, distance, side effects, stigma and discrimination [22] and a poor adherence for both diseases is a sine qua non for poor prognosis. TB patients with CD4>200 had more complete cure rate. This is consistent with other findings, as starting treatment at a better CD4 count is generally associated with better prognosis [23] TB patients with pulmonary disease had better cure rates (Fig. 5) [24].

5. CONCLUSION

This evaluation identified critical gaps in context and systems for the management of TB and HIV in the facilities and levels of care assessed. It is

strongly advisable that government at all levels draft and circulate checklist that monitor administration of infection control practices across the three levels of care to promote adherence. Infection control guidelines and processes should be established and monitored for implementation at the PHC level. Strengthen tracking of referrals using a locked referral directory that checks and documents referral arrivals and obtains feedback from the referral destination; institute sample transport system to remove all the observed gaps in TB case finding among PLHIVs, from screening to diagnosis. There should be fidelity of TB screening on the ART care card, to effectively identify and deal with presumptive TB cases, and track the TB/HIV cascade in a timely manner. Despite the benefit of the test and treat policy, diagnosed TB and HIV co-infected patients should be well counselled on the benefits of immediately starting ART, but this should be considered with patient choice.

CONSENT

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

ETHICAL APPROVAL

The study proposal was submitted to the University of Calabar Teaching hospital and the Cross-River State Ministry of Health Review Board (IRB) for review and thereafter received ethical clearance from both review boards.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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Peer-review history:
The peer review history for this paper can be accessed here:
http://www.sdiarticle4.com/review-history/61152