



Intensified TB Case finding in PMTCT settings in Nigeria should be reconsidered

***Odo,Michael¹,Obeagu,Emmanuel Ifeanyi², Ochei, Kingsley Chinedum¹, Nkombe, Emmanuel³, Olusola-Falae, Bolanle⁴, Effa, Emmanuel³ and Affirima, Barinaadaa³**

¹Department of Prevention Care & Treatment, FHI 360 Country Office, Area 3 Garki Abuja.

²Diagnostic Laboratory Unit,Health Services Department,Michael Okpara University of Agriculture,Umuahia,Abia State Nigeria.

³Department of Prevention Care & Treatment, FHI 360 Cross River state office, Calabar.

⁴Department of Prevention Care & Treatment, FHI 360 Lagos state office, Lagos

***Corresponding author**

Abstract

Resources are scarce to meet the ever growing challenges of TB and HIV in Nigeria. Nigeria ranks 3rd among the 22 high burden TB countries, with estimated TB prevalence rate of 322/100,000 and an HIV sero-prevalence rate of 4.1%. The first ever TB prevalence survey conducted in Nigeria in 2012 estimated the TB/HIV co-infection rate of 25% in the country. TB/HIV collaboration has been shown to increase TB and HIV case finding among both groups. Intensified TB case finding has been established in HIV counseling and treatment sites but not in PMTCT settings in Nigeria. HIV-infected pregnant women are ten times more likely to have active TB than HIV-uninfected pregnant women and TB has serious implications during pregnancy. Antenatal care (ANC) is an important point of contact between pregnant women and the health system. This paper describes a pilot intervention for intensify TB case finding among antenatal attendees in four facilities providing PMTCT services in Nigeria. This was a cross-sectional operational study from May to October, 2012. Health providers at ANC, DOTS clinics and the AFB/GeneXpert laboratory received orientation on TB/HIV collaboration and referrals. The HCT client intake form with WHO TB symptoms screening checklist was modified to include pregnancy related indices for screening of TB among pregnant women attending ANC. The clients with a score of ≥ 1 were referred for AFB microscopy or GeneXpert machine. Results were entered into a modified ANC register from which a monthly summary was derived. Out of the 2793 pregnant women clinically screened for TB, 189 had a score of ≥ 1 . Only 103 out of the 189 women had productive cough and 64 were tested using AFB microscopy while 39 were tested with GeneXpert. Only one pregnant woman was diagnosed with active TB (sputum smear positive) and was referred to the DOTS clinic for anti-TB treatment. Intensified TB case finding in PMTCT setting appears to be a low yield intervention and may not be cost effective. It however provides an opportunity for TB awareness and education.

Keywords: TB ,HIV/AIDS,PMTCT SETTING,Genexpert,AFB.

Introduction

HIV infection increases the risk for Tuberculosis (TB) significantly either because of reactivation of latent infection or progression of newly acquired infection with tubercle bacilli. Women of reproductive age have a higher biological and social vulnerability to the acquisition of HIVⁱ (Joint United Nations Programme, 2011) and contribute significantly to the

number of people infected with HIV and TBⁱⁱ (who,2009). Consequently, HIV/TB co-infection is gaining ground as a leading cause of both obstetric and non-obstetric mortality and morbidity among women in resource poor settings with high HIV prevalence rates like the Sub-Saharan Africaⁱⁱⁱ,^{iv} (Ahmed *et al.*,1999;Khan *et al.*,2001). Globally, an estimated 700,000 women died from TB in 2008 compared with

an estimated 342, 900 who died from maternal causes in the same yearⁱⁱ (who,2009). In Nigeria, the incidence of TB increased from 2.2% to 25% between 1991 and 2010 mainly due to HIV infections^v, with a TB/HIV co-infection rate of 25%.

TB in women of reproductive age has serious implication during pregnancy. HIV infected women with TB have lower CD4 counts compared to those without TB^{vi} (Kali *et al.*,2006). Similar to HIV, TB may also be vertically transmitted in utero, intra partum and postpartum^{vii} (Pillay *et al.*,2004). Even in the absence of vertical transmission, TB in pregnancy has critical impacts on perinatal outcomes. TB causes intrauterine growth retardation, low birth weight, prematurity and increases the risk of HIV acquisition in a newborn of a HIV infected mother^{viii} (Lin *et al.*,2010).

Although, the consequences of TB among women of reproductive age have been recognized, TB cases continue to go undetected among women. In 2004, the World Health Organization (WHO) reported that the number of smear-positive case notifications in adult women (aged 15 years and over) was 10% lower than that in adult men^{ix} (WHO,2006). A population based study in Vietnam also showed a significant under-detection of TB cases among females in the National TB program^x (Thorson *et al.*,2004). In this study, Case detection was estimated to 39% (95% CI 20–76%) among men and 12% (95% CI 6–26%) among women. Considering the impact of TB during pregnancy and low detection of TB cases among women, it is important to investigate for TB among pregnant women accessing ANC particularly in resource poor settings. Although, there is some documentation on intensified TB case finding among women in some parts of Africa^{v,x,xii} (United Nation Embassy in Nigeria,;Gounderet *al.*,2011;Nacheda *et al.*,2003), such empirical evidence is yet to be elucidated in Nigeria. This underscores the need to investigate the pattern of case finding among pregnant women in Public Health facilities in Nigeria.

Antenatal care is an important point of contact between women and the prevention of mother to child transmission of HIV (PMTCT) services. WHO recommends intensified TB case finding during HIV testing and counseling, and anti-retroviral therapy clinics. PMTCT programs conducted in these clinics offer a unique opportunity to test large numbers of women of reproductive age for HIV as well as implement TB screening using the recommended WHO clinical algorithm for TB screening.

Unfortunately, the Nigerian PMTCT program does not routinely do clinical screening of TB among pregnant women.

The public health facilities with support from PEPFAR and Global fund are the highest provider of HIV prevention, care and treatment services as well as integrated maternal and child health care services in the country. TB case finding, prophylaxis and treatment are an integral part of these services. Therefore, the public sector offers a huge opportunity to investigate the feasibility of integrating PMTCT/TB services among pregnant women.

In this study, we conducted a cross-sectional operational study across 6 public health facilities from each geopolitical zone to actively screen pregnant women who are assessing ANC/PMTCT services in public health facilities supported by the Strengthening Integrated Delivery of HIV/AIDS Services, Nigeria (SIDHAS). By revealing TB case finding patterns, this study will improve TB case detection among pregnant women and accelerate the achievement of the health related Millennium Development Goals.

TB/HIV CO-INFECTION

Both TB and HIV have dire consequences on the immune system of the human host and exacerbate each other's pathological effects when they co-exist^{xiii} (Pawlowsk *et al.*,2012). HIV is a known risk factor for latent TB reactivation and progression to active disease while TB has been reported to aggravate HIV infection^{xiii} (Pawlowsk *et al.*,2012).

CD4⁺ T-cell depletion which is a chief feature of HIV's attack on the immune system causes reactivation of latent TB and susceptibility to new infection^{xiv} (Lewinsohn *et al.*,2007). It also interferes with granuloma formation and thereby exacerbates the systemic spread of TB, thereby, giving rise to multi-systemic and disseminated TB^{xv} (Rosa-Taraco *et al.*,2006). Other suggested mechanisms include up-regulation of Mycobacterium Tuberculae entry receptors in macrophages^{xvi} (Wahl *et al.*,1989), impairment of macrophage bactericidal pathway^{xvii} (Spear *et al.*,1990) and chemotaxis^{xviii} (Wahl *et al.*,1989). Mycobacterium tuberculosis infection on the other hand has been reported to induce up-regulation of HIV replication in T-cells and macrophages^{xix} (Patel *et al.*,2007). In order to reduce the deleterious effects of TB/HIV co-infection, the WHO has recommended TB/HIV collaborative

programs to help quell morbidity and mortality due to both infections^{xx} (Nakata *et al.*,1997). These programs include intensified case finding among people living with HIV, infection control in TB, isoniazid prophylactic treatment and provision of antiretroviral drugs.

INTENSIFIED TB CASE FINDING AMONG PEOPLE LIVING WITH HIV

Intensified case finding of TB involves asking symptom screening questions for TB during clinical visits, conducting an appropriate TB diagnostic test for anyone with a positive symptom screen, and performing TB contact screening for household members of all index patients^{xxi} (WHO,2011). Intensified case finding of TB is aimed at early detection, increasing chance of survival in TB infected individuals and reducing rate of transmission among the general population^{xxi} (WHO,2011). This intervention is particularly important for people living with HIV.

The WHO 2011 guidelines on ICF and IPT in HIV settings recommends the use of a simplified clinical screening algorithm based on four symptoms to identify individuals eligible for further diagnostic work up and IPT^{xxii} (Kim *et al.*,2012).The symptoms screened for include current cough, fever, weight loss and night sweats. It is recommended that adults and children PLHIV with no symptoms be given isoniazid prophylactic treatment while those with any of the four symptoms should undergo further diagnostic TB based on National guidelines^{xxi} (WHO,2011). Evaluation studies support that intensified TB case finding in HIV care is operationally feasible and beneficial to both patients and health system^{xxiii} (Elden *et al.*,2011).

INTEGRATING ANC, PMTCT AND INTENSIFIED TB CASE FINDING

HIV/TB co-infection is gaining ground as a leading cause of maternal mortality in resource poor settings with high prevalence rates of HIV. A study from South Africa showed that HIV-infected pregnant women were ten times more likely to have active TB than HIV-uninfected women^{xxiv} (Pillay *et al.*,2001). These findings are also supported by a cross-sectional study conducted in the same country among HIV infected women in two public health clinics showed that 32% of the study population had symptoms

suggestive of TB with 2.16% prevalence of active TB^v (United States Embassy in Nigeria,). In a tertiary hospital in South Africa, a study assessing the prevalence of TB among HIV-infected, tuberculin skin test positive women who had just delivered showed that 50% of them had latent TB while 11% had active TB^{xi} (Gounder *et al.*,2011).

TB in women of reproductive age has serious implication during pregnancy. HIV infected women with TB have lower CD4 counts compared to those without TB^v (United States Embassy in Nigeria,). Similar to HIV, TB may also be vertically transmitted in utero, intra partum and postpartum. A prospective case series of pregnant women diagnosed with TB showed 16% risk for vertical transmission of TB^{vi} (Kali *et al.*,2006). Even in the absence of vertical transmission, it also has critical impacts on perinatal outcomes. TB causes intrauterine growth retardation, low birth weight, prematurity and increases the risk of HIV acquisition in a newborn of a HIV infected mother.

Antenatal care is an important point of contact between pregnant women and the public health care system particularly in resource poor settings where access to health services is low. This is because it provides an opportunity to screen large number of women for both HIV and TB and offer lifesaving interventions for both diseases. Operational evidence from South Africa demonstrated the feasibility of integrating PMTCT and intensified TB case finding as well as the challenges encountered during implementation of such programs in public health settings.

REASON FOR THE INTERVENTION

Although, the benefits of intensified TB case finding as well as its integration into PMTCT have been documented in other parts of Africa, there is dearth of evidence on the prevalence of TB among both HIV infected and HIV uninfected mothers as well as feasibility of integrating PMTCT and ICF in Nigeria. This study provides an opportunity to validate the WHO algorithm in pregnant women as suggested by Gounder *et al*^x (Thorson *et al.*,2004).

Kali 2006^v observed a low level of acceptance for TB symptom screening among HIV positive pregnant

women during post HCT sessions. The study argues that conducting TB screening during the pre HCT session targeting both HIV-infected and HIV-uninfected expectant women may increase acceptance for TB screening among women and improve TB case detection during pregnancy. This study sought to implement TB case finding during the pre HCT session and assess the level of acceptance and case detection during this period.

By assessing the effectiveness and feasibility of combining intensified TB case finding and PMTCT in Nigeria using WHO ICF algorithm and Xpert MTB/RIF, this study will address the gaps in existing evidence on ICF and improve TB case detection among pregnant women.

The program will be implemented in line with SIDHAS and NTBLCP strategy on ICF. We will take sustainability of the program into consideration by using existing HCT and TB focal persons in the health facilities where the program will be implemented.

OBJECTIVE

The primary objective of this study is;

1. To identify the number of TB suspects
2. To identify the number of TB cases
3. And secondarily we assessed the feasibility of integrating intensified TB case finding with PMTCT and ANC by measuring the following outcomes;
4. Number of women who received TB symptom screening per visit for the duration of the study
5. Number of suspects from whom sputum was successfully collected and screened using Xpert MTB/RIF
6. Number of identified TB cases that were successfully referred to TB centres for care and treatment.

Materials and Methods

Study Design:

This was a cross-sectional operational study

Study Duration

The study will take place from May to October, 2012.

Setting and Context

In Nigeria, the national HIV and TB-control programs were largely managed as parallel vertical programs. With increasing rates of TB/HIV co-infection in Nigeria, programme collaboration became necessary. However, the integration of TB in HIV services did not happen in PMTCT settings; hence no form of TB service is available in antenatal care settings. The PMTCT services in Nigeria are integrated in the routine antenatal care services of primary, secondary and tertiary health care facilities. These services are provided by qualified nurses and Community Health Workers depending on the cadre of the facility.

The strengthening Integrated HIV/AIDS Services (SIDHAS) is a 5-years project funded by the United States Agency for International Development (USAID) under the Presidents Emergency Plan for AIDS Relief (PEPFAR) and started in 2011. SIDHAS supports antiretroviral therapy (ART) in 315 and PMTCT 2750 sites in Nigeria. Only three of the Four (4) high volume pilot PMTCT sites (State Specialist Hospital, Yola, General Hospital, Ajeromi and Murtala Muhammed Specialist Hospital, Kano) supported by SIDHAS, and in close proximity to Xpert MTB/RIF sites were purposefully selected to participate in the study.

Pregnant women attending ANC clinics were provided HIV counselling and testing, and also screened for TB using the WHO symptoms screening checklist. Clients with a positive TB screening score (a score of ≥ 1) were referred for a sputum diagnostic test using AFB microscopy and GeneXpert where it was available. The outcomes of the TB screening and sputum diagnosis were entered into structured national data collection tools clients which will be modified to capture these additional information that are not currently routinely captured.

TB case finding in HCT clinics – description of the integration model

The antenatal care nurses who provide the PMTCT services were offered a 2-day training on HCT/TB screening tool, ICF and data collection using the TB/HIV national guidelines. The national HCT client intake form was revised and administered to all pregnant women attending first ANC clinic visit. A client that answers “yes” to any of the 5 questions is considered “TB suspect” and referred to the laboratory for confirmatory AFB sputum test. On the spot collection of sputum sample for diagnosis from all

identified TB suspects was done. The samples were transported weekly from the study site to AFB and/or Xpert MTB/RIF sites. Diagnosed TB and HIV cases

were referred for management with DOTS and ART. Monthly supervision and data collection was conducted by Local Government TB Supervisor.

Table 1: Checklist for TB Clinical Screening

Clinical TB screening		
Coughing for > 3 weeks	[0]	[1]
Weight loss of ≥ 3 kg in last 4 weeks	[0]	[1]
Lymphadenopathy (<i>swelling of the lymph nodes</i>)	[0]	[1]
Fever for > 2 weeks	[0]	[1]
Night sweats for > 2 weeks	[0]	[1]
TB screening score: (calculate the sum of the 5 answers above) If score ≥ 1 , test for sputum AFB or refer to TB service	□	

Each of the PMTCT clinics was supplied with TB job aids, referral forms, TB/HIV SOPs and M&E tools. The HCT client intake form and facility ante natal register were modified to capture information on the TB status of the pregnant women. Clients who test positive for AFB or GeneXpert sputum test are started

on TB treatment in the DOTS clinics co-located in the health facility, irrespective of HIV status. Only SS(+) HIV positive clients in this facilities were referred for these test to rule out active TB. Monthly supportive supervision was provided by the project staff to facilitate the process.

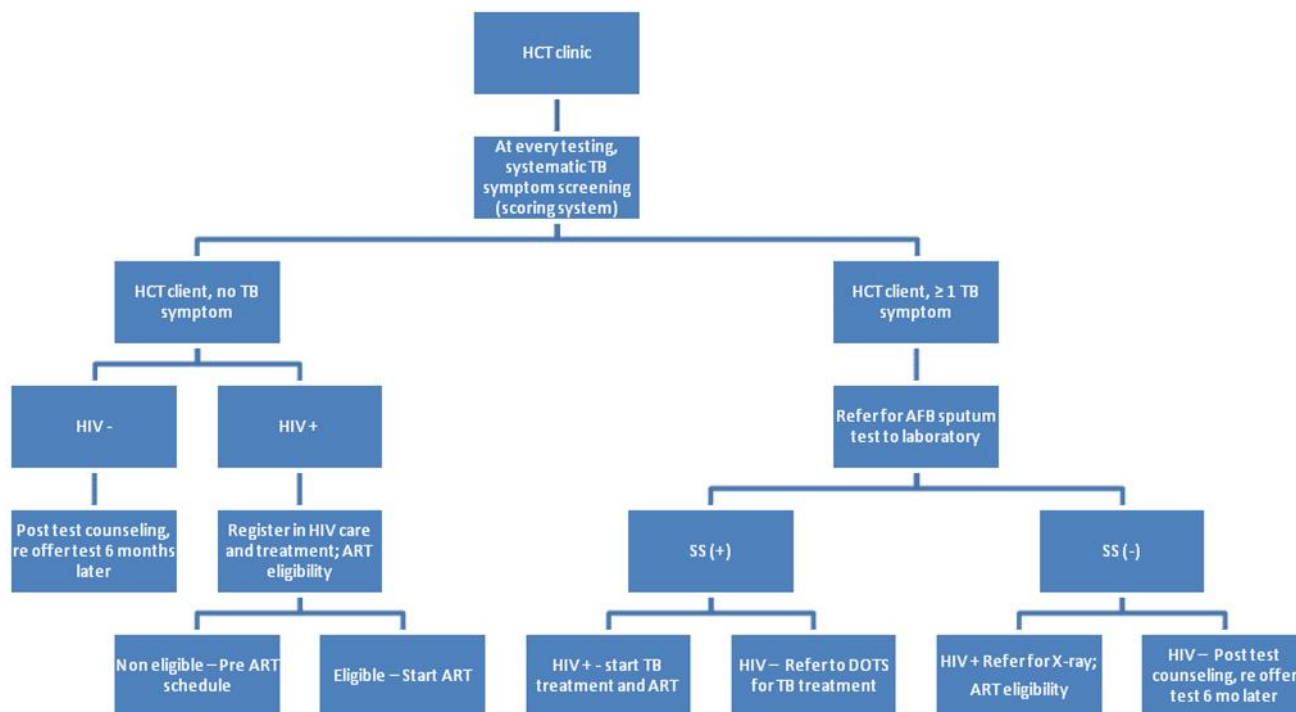


Figure 1: – Integration model in GHAIN supported sites

Study Population

All pregnant women attending the ANC/PMTCT service during the study period. Pregnant women presenting with obstetric, gynecological or medical emergencies were excluded from the study.

Data Collection Tools

- 1) Modified ANC Counseling and testing register.
- 2) The TB lab register which contains information on the result of sputum TB diagnostic test.
- 3) The TB treatment register which contains information of TB diagnosed patients enrolled in TB DOTs treatment program.

DATA MANAGEMENT

Routine ANC records and records on TB screening and diagnosis extracted from the modified national DCT were entered into a Microsoft Excel spreadsheet® designed for the data entry and cleaned for consistency. The cleaned data was exported to STATA version 10.0 (Stata Corporation, College Station, TX) for data management and statistical analysis. Frequency counts will be performed to assess for completeness of all variables. A positive TB screening score that is, a TB screening score of ≥ 1 and a positive sputum TB diagnosis were the major outcome variable in this study. These were determined for all pregnant women attending ANC clinics and for the subset of those with a significant TB screening score. The rates for significant screening score and positive TB diagnosis along with the 95% confidence intervals will be estimated for the study population as well as for the sub-population of HIV positive pregnant women. Correlates of TB diagnosis will be assessed by multivariable logistic regression. Hosmer and Lemeshow test was used to check for how well the model fit. All tests will be two-sided and statistical significance will be set at p value < 0.05 . Differences in proportions will be tested using Chi-square test.

Ethical Consideration

Ethical approval was from National Ethical committee and FHI360 IRB. Confidentiality and privacy of medical records will be maintained. This will be an evaluation or audit of routine service delivery of SIDHAS TB/HIV program and so informed consent will not be sought from participating patients.

Results

Pre-tested HCT and WHO TB clinical screening checklist was successfully integrated into PMTCT schedule in the pilot ante natal clinics. A total of 2,793 pregnant women were offered HIV counselling and testing and clinically screened for TB.

Of the number of Pregnant women screened, 189 had a WHO TB screening score of ≥ 1 . Only 103 out of the 189 women had productive cough and were referred for investigation.

Of the number referred for investigation, 64 were tested using AFB microscopy while 39 were tested with GeneXpert based on availability. One pregnant woman was smear positive for TB and was referred to the DOTS clinic for anti-TB treatment. None of this women was HIV positive.



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Discussion

A large number of pregnant women gather in these clinics monthly through the period of gestation and this provides a huge opportunity for clinical screening and laboratory investigations. Nigeria contributes 30% of the global gap in the prevention of mother to child transmission of HIV (PMTCT), and has drawn significant attention and resources from the Global Fund (GF) against HIV, and the US Presidents Emergency Plan for AIDS Relief (PEPFAR). In recent times, with an over bearing high TB burden with an incidence of 388/100,000 and a low case detection of 17% (NSP 2015-2020), there is pressure to introduce TB screening and investigation as part of the required services in antenatal care. We studied the introduction of TB screening tools and TB microbiological investigation in selected PMTCT settings.

The integration of the modified Client intake form (CIF) for routine TB clinical screening and microbiological investigations for mycobacterium TB, into HIV antenatal care services in the selected facilities in Nigeria was feasible and received high acceptance among the health workers and the pregnant women. Although, the integration effort provided a platform for medical education and awareness on TB transmission and treatment, it did not appear to increase detection of TB cases among the pregnant women seen in the study. Only 189 (6.8%) of the 2,793 pregnant women were clinically screened for TB had presumptive TB. Upon investigations with AFB microscopy and GeneXpert, only one of them had TB disease.

In this study it was possible to analyze the aggregate data from the PMTCT settings that were identified as presumptive TB cases, but, not all the pool of Pregnant women with presumptive TB were able to produce sputum. In addition, in places where only AFB was available, there was no progression to repeat the test with a GeneXpert. Only 39 (37.9%) of the 103 women who had productive cough were tested with GeneXpert, with only one woman coming down with TB disease.

Sustaining TB/HIV program integration across policy and service delivery systems is globally recognized as a key strategy for improving TB case detection, reducing co-morbidities and mortality, and treatment outcome among PLHIV (WHO, 2006). The use of TB clinical screening strategies in HTC centers to improve TB case detection has been documented outside Nigeria (Gounder *et al.*, 2011). A large percentage of patients presenting at HTC centers in developing countries may have active tuberculosis because of the high rate of HIV and tuberculosis co-infection as well as overlap between HIV symptoms and those of Tuberculosis (Nachada *et al.*, 2003). As a result, HTC centers have been identified as a good setting to identify large numbers of individuals with active tuberculosis (Gounder *et al.*, 2011). In Nigeria, the previous parallel operation of the TB and HIV programs was an obstacle to integration services and a problem to TB case detection among PLHIV. The proportion of TB suspects identified among the PMTCT clients using the combination of clinical indices on the modified CIF form in this study is 6.8%.

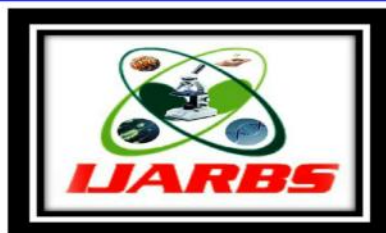
Conclusion

This study confirms that in resource limited settings with a high HIV and tuberculosis prevalence, TB screening initiated through PMTCT is feasible and important in providing a platform for the sharing of TB messages that could spread quickly to households and the community. However, the low numbers of presumptive TB cases and TB cases found among these groups of pregnant women suggest TB screening in the PMTCT setting is a low yield intervention, and should be reconsidered.

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