

Original Article

Treatment Outcomes among Human Immunodeficiency Virus and Tuberculosis Co-Infected Pregnant Women in Resource Poor Settings of South-western Nigeria

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ABSTRACT

The complex interactions between Human Immunodeficiency Virus (HIV) and Tuberculosis (TB) infections may be magnified, in the presence of another potentially stressful condition like pregnancy. Though co-infection among pregnant women is rare, treatment outcomes may depend on accessibility to comprehensive treatment modalities. The objective of this study is to determine treatment outcomes among pregnant HIV and TB co-infected pregnant women in Lagos, South-western Nigeria. This retrospective, analytical study was carried out among ninety four (94) eligible pregnant women co-infected with HIV and TB at selected health-care facilities in Lagos state between January, 2008 and December, 2009. A standard checklist for data collection was used and analysis was carried out using the EPI info software. Mean age of respondents was 30.8 (± 3.9) years. Sixteen (17.1%) TB cases were clinically diagnosed for tuberculosis. Among tuberculosis cases identified through sputum microscopy, 60(63.8%) were acid fast bacilli (AFB) positive and 21(22.3%) were identified in the first trimester. The mean percentage adherence to anti-retroviral drugs was 95.9% (± 5.3). None of the participant smoked cigarette. Seventy three {73 (77.7%)} had contact with TB infected or suspected person in the last three months. Treatment outcome in mother showed that 74(78.7%) were cured, 8(8.5%) relapsed while 12 (12.8%) had treatment failures. Among the babies, 83(88.3%) were born alive. Women with both poor adherence (<90%) and with positive TB contact, but neither factor alone, were half-fold less likely to be cured compared with women with both good adherence (>95%) and no TB contact (OR=0.59, CI=0.45-0.95 and $p=0.014$). Cure rate was substantially lower in this study. This calls for extra strategies such as routine TB screening in antenatal clinics, strict adherence to national guidelines in the treatment of HIV/TB co-infections, focused antenatal care and comprehensive Prevention of Mother to Child Transmission (PMTCT) care and treatment.

Keywords: Adherence, HIV/ TB co-infection, Pregnancy, Treatment outcomes,

Received 08 June 2011/ Accepted 19 September 2011

INTRODUCTION

A steady association between Human Immunodeficiency Virus (HIV) and Tuberculosis (TB) infections has been widely documented. Over nine million new cases of tuberculosis (TB) occur annually throughout the world. While most of these cases can safely and effectively be treated, complications can occur during TB treatment, because of anti-TB drug resistance, poor

adherence, drug-drug interactions, and toxicity (Whalen, 2007). Human Immunodeficiency Virus (HIV) has contributed to a global resurgence of tuberculosis (Corbett *et al.*, 2003). In Sub-Saharan Africa, the prevalence of HIV is about 5%-35% of the adult population, and one-third to one-half of HIV-infected individuals is co-infected with *Mycobacterium tuberculosis* (WHO, 2006). Women are special group at risk for contacting these

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infections. Pregnant infected women are however at a greater risk because the physiological state of pregnancy could be overwhelming with stress which may further compromise an already depleted immune status. The two most common opportunistic diseases encountered in HIV-related lung complications during pregnancy are infection with *Pneumocystis jiroveci* and *Mycobacterium tuberculosis* (Saade, 1997).

The effects of TB on pregnancy depend upon various factors such as type, site and extent of the disease, stage of pregnancy when management gets instituted, nutritional status of mother, presence of concomitant disease, immune status and co-existence of HIV infection, availability of facilities for early diagnosis and treatment (McIntyre, 2003; Loto and Awowole, 2011). In a South African study, TB was the third leading cause of maternal mortality; mostly in combination with HIV-infection (Khan *et al.*, 2001). It is also the most common cause of deaths in HIV-positive adults living in developing countries, despite being a preventable and treatable disease (Corbett *et al.*, 2003). Fifty four per cent maternal deaths caused by tuberculosis were attributable to Human Immunodeficiency Virus-1 infection (Khan *et al.*, 2001). Increased susceptibility to TB complications may continue to be a major cause of maternal mortality in high prevalence HIV areas (Pillay *et al.*, 2001; Corbett *et al.*, 2002).

However, some studies have shown that pregnant patients with active tuberculosis may only have few of the typical symptoms (Carter and Mates, 1994), thus stressing the need for a high index of suspicion by care providers. There is general agreement that appropriately treated tuberculosis does not worsen the outcome of pregnancy. Tuberculosis that developed during pregnancy can be successfully treated without harm to the developing foetus if diagnosed early enough. If anti-tuberculosis treatment (ATT) is started early in pregnancy, the outcome would be the same as for non-pregnant patients, whereas late diagnosis and care is associated with 2-fold increase in obstetric morbidity such as pre-maturity and low birth weight (WHO, 2002). Besides, the availability of appropriate diagnostic/therapeutic facilities and/or affordability of their use tend to result in poor management and outcome in pregnancy. Treatment requires a coordinated multidisciplinary approach to ensure that the best

management is offered and that compliance with medication is maintained.

Depending on CD4 count and gestational age at initiation of treatment, ART treatment regimen for HIV positive pregnant women usually combine first line antiretroviral drugs such as Zidovudine, Lamivudine, nevirapine or Efavirenz or a Tenofovir based regimen. Anti-TB drugs include isoniazid and rifampicin, pyrazinamide and ethambutol based regimen to be given in the initiation phase and isoniazid and ethambutol in continuation phase of DOTS therapy (FMOH, 2005). However, since several women in developing countries do not have access to prompt and complete treatment and even PMTCT. The true prevalence of coexisting TB and HIV among pregnancy may not be ascertained in many countries and may require extensive research, though most literature testified to the rarity of the presentation.

Nigeria has the fourth highest burden of tuberculosis (TB) in the world, with an annual incidence of 311 cases per 100,000 population and a mortality rate of 81 per 100,000 population in 2006 (WHO, 2008). Nigeria also have HIV seroprevalence rate of 4.4%, the third highest infection burden in the world while about 21% of all TB patients are dually infected with TB and HIV (Ref). With the advent of the Directly Observed Treatment Short Course) DOTS initiated by the National Tuberculosis and Leprosy Control Program (NTBLCP) in 1993 to streamline treatment and coordinated efforts at TB surveillance, case detection rate in Nigeria was 23% while treatment cure rate was as high as 76%. This appreciable cure rate of TB cases using DOTs is not only in Nigeria, but virtually all countries where the strategy has been holistically adopted (WHO, 2006).

Nevertheless, records of TB and HIV co-existing in pregnancy are not readily available routinely in Nigeria. The paucity of data on this subject could attest to rare presentations of TB and HIV co-infections among pregnant women. Situation is worsened by the growing cases of multi drug resistant TB in the face of antiretroviral drugs and changing prevalence of HIV epidemics. It is thus important to examine possible influence of pregnancy state on outcomes of DOTS programme which as at present exists in virtually all the 774 local government area councils in Nigeria.

The objective of this study is to determine treatment outcomes among pregnant co-infected TB and HIV client in Lagos in South-western Nigeria.

METHODOLOGY

Study Design and Site

This is a retrospective, analytical study of treatment outcomes among pregnant co-infected HIV-TB clients seen in selected general hospitals in Lagos state between January, 2008 and December, 2009. In Lagos state, most general hospitals have projects supported by donor agencies, with standard DOTS programmes integrated into HIV treatment and control programmes. Donor agencies usually provide HIV test kits, ARVs and related logistics. The National Tuberculosis and Leprosy Control programme under Federal Ministry of Health is the major source of supports for DOTs programmes in Nigeria.

Division of facilities or sites into comprehensive or stand alone has been the major responsibility of Lagos State Action Committee on HIV/AIDs based on ability to manage HIV and co-infections in pregnancy. Ten out of fourteen general hospitals in the state designated as comprehensive sites (with resources to manage both HIV and TB co-infection treatments) were randomly selected for this study. Eligibility criteria include all respondents that were pregnant, HIV positive, enrolment into facility PMTCT care, and those with no other obstetrics diseases or diagnosis. All eligible cases seen within the period were reviewed because of perceived rare presentation of TB and HIV co-existing in pregnancy. Ethical approval was obtained from the hospital authority and ethical review committee of the state hospital management board.

HIV Testing

HIV infection was diagnosed among the pregnant women using the national serial algorithm HIV testing method which employs the use of rapid test kits for screening and confirmation (FMOH, 2003). Three test kits were in the serial algorithm. "Determine" (Abbot Diagnostics) was first used on the sample and if non-reactive or negative, further testing stops at this stage. If reactive, "UniGold" (Trinity Biotech USA) was then used for confirmation. Discordant result was resolved with "Startpack" (manufactured by Chembio Diagnostics Systems) and the outcome of this test kit and "Determine" was accepted as the final result.

TB diagnosis

Tuberculosis were diagnosed either using sputum microscopy or clinically with a high index of suspicion among clients with persistent cough of more than three weeks and other signs and symptoms (FMOH, 2005). A clinical diagnosis of TB was based on history of persistent cough for a period of three weeks or more and not responding to conventional antibiotics. Adherence to medications was measured by making enquiries from clients, through routine monthly pill counts and review of pharmacy pick-up records. Though adherence of 100% is always the target while managing clients, missing drugs one or twice in a month usually attract about 95%, three to four attracts 91 to 95, while missing pills 5 or more times in a month usually attracts adherence score of or less than 90% (NACA, 2005). Case notes of all 96 newly diagnosed for TB clients seen within the study period were reviewed at the PMTCT and DOTS clinics, and secondary data such as socio-demographic characteristics and treatment outcomes for TB in the mother were obtained using a standard checklist designed to collect data from case notes.

Measurement of Treatment Outcomes

Treatment outcomes were measured at the completion of the eight months DOTS regimen when clients would have been re-assessed for TB diagnosis, either to have been cured, treatment failure, relapse or as the case may be. Data was analysed using EPI Info software, and frequency tables generated. Associations between categorical variables were computed at a significant *P* level less than or equal to 0.05. Odds ratios values were computed to determine cause-effect associations between relevant variables that may contribute to occurrences of mortality and morbidity.

RESULTS

Out of the 96 cases, 94 (97.9%) had complete management data evident for a period of about one year after commencement of treatment, and their case notes were analysed. The remaining two unanalysed though diagnosed were lost to follow up, with no record of continued medications or treatments and no delivery or post - partum records in the health facility. Table 1 shows the socio-demographic characteristics of respondents. Seventy (74.5%) respondents were in the age group

25 to 34 years. The mean age was 30.8 (± 3.9) years. Eighty one (86.2%) respondents were married while 8 (8.5%) were single. About 61 (64.9%) had secondary education. Table 2 shows that only 16 (17.1%) were clinically diagnosed for tuberculosis, while the rest were identified through sputum microscopy. Among those identified through microscopy, 60 (63.8%) were AFB positive. Twenty one (22.3%) were identified in the first trimester while 56 (59.6%) were identified in the second. Level of adherence to anti-TB and ARVs medications was assessed to be as high as above 95% among 58 (61.6%) respondents.

Table 1: Biodata of Respondents

Biodata	Frequency (%)
Age	
15-24	0(0)
25-34	70(74.5)
35-44	24(25.6)
Marital Status	
Married	81(86.2)
Single	8 (8.5)
Others	5 (5.3)
Education Level	
Primary	28(29.8)
Secondary	61(64.9)
Tertiary	5(5.3)

Table 2: Treatment Outcomes in TB-HIV Co-infected Pregnant Women

Variable	Frequency (%)
Mode of Diagnosis	
Clinical	16(17.1)
Sputum AFB	78(82.9)
Sputum AFB results (n=78)	
Positive	60(76.9)
Negative	18 (23.1)
Time of diagnosis	
First trimester	21(22.3)
Second trimester	56(59.6)
Third trimester	17 (18.1)
Adherence to Anti TB Drug/Anti-retroviral	
90 and less	24(25.6)
91-95	12(12.8)
96-100	58(61.6)
Risk Factors for TB (Yes option only)	
Respondent smokes cigarette	0(0.0)
Had contact with TB infected person in the last 3 months	73(77.7)
Outcomes of TB in Mothers	
Cured	74(78.7)
Relapsed	8(8.5)
Treatment failure	12(12.8)
Outcomes of babies at birth	
Alive	83(88.3)
Dead	11(11.7)

The mean percentage adherence was 95.9 (± 5.3). None of the participants smoked cigarette. Seventy-three (73) (77.7%) had contact with TB infected or suspected person in the last three months. Treatment outcome in mother shows that 74 (78.7%) were cured, 8 (8.5%) relapsed while 12 (12.8%) had treatment failure. 83 (88.3%) babies were born alive.

Further analysis shows that a significant association exists between treatment outcome in mothers and age of mother with AFB ($N=60$, $X^2=94.0$, $p=0.001$), level of adherence with drugs ($N=58$, $X^2=71.0$, $p=0.001$) and outcome of babies at birth ($N=41$, $X^2=31.8$, $p=0.003$). Further logistics regression analysis showed that women with both poor adherence ($<90\%$) and with positive TB contact, but neither factor alone, were half fold less likely to be cured compared with women with both good adherence ($>95\%$) and no TB contact ($OR=0.59$, $CI=0.45-0.95$, $p=0.014$)

DISCUSSION

In this study, few clients were clinically diagnosed through persistent cough and or haemoptysis and other typical presentations. Among clients identified by sputum microscopy, about two thirds were positive for AFB. Diagnosis by X-rays may not feature among these pregnant clients because of potential teratogenicity of X-rays in pregnancy. A delay in diagnosis of TB in pregnancy could however occur if clinicians continue to wait for a history of protracted episode of coughing, instead of a high index of suspicion for tuberculosis in clients with a history of cough in addition to some other clinical signs and symptoms.

Many clinicians would usually confirm their clinical diagnosis by sending clients for sputum microscopy, since TB screening is not mandatory for all women in pregnancy. A possible argument is to assess the clinical judgment on a single positive sputum microscopy as opposed to three positive tests, but this calls for more research regarding its validity in correctly diagnosing tuberculosis in pregnant women. The cure rate observed in this study is low when compared with the WHO target of achieving 85% cure rates using DOTs strategy (WHO, 2008). Among TB-HIV/TB co-infected non-pregnant clients in Nigeria, a cure rate of 12.7% was reported (Njebuome and Odume, 2009). The study further reported that the default rate was higher among the clients co-infected with HIV.

Another African study also suggested that TB patients co-infected with HIV had worse treatment outcomes (Rustomjee *et al.*, 2004). Although, no death was reported in this present study as supported by another study (Jana *et al.*, 1994), high maternal mortality has been associated with puerperal women with TB and those with HIV co-infection (Ormerod, 2001; Khan *et al.*, 2001). Our observation may be as a result of the relatively low sample size with limitations such as inability to include cases of extra-pulmonary TB, inability to study drug resistance and treatment outcomes among babies. Additionally, the retrospective nature of the study made it inconclusive to fully ascertain the actual number of women with confirmed cases of TB using sputum microscopy as standard, and the actual number of non-smokers based on extent of documentations. Therefore, there is a need to carry out more extensive research on the subject.

Adherence in this high-risk group is important to improve clinical outcomes as well as prevent Multi-Drug Resistance (MDR) that could cause relapse and high failure rates (Paterson *et al.*, 2000; Abaasa *et al.*, 2008, Mellins *et al.*, 2008). In this study, there was an association between adherence to anti-retroviral drugs and anti-TB and outcome of treatment in mothers. Treatment outcomes might have improved because of a continuing emphasis on serial adherence counselling sessions adopted in most PMTCT programmes on the use of both ARVs and anti-TB drugs, strong political will of stakeholders to supply drugs and logistics, as well as strong commitment of relevant health care workers.

Nevertheless, about one fifth was found to have relapsed or had treatment failure. This is comparative to figures reported by other Nigerian authors (Lawson *et al.*, 2010; Lawson *et al.*, 2011) but more importantly suggested that MDR-TB is gradually becoming an issue in many countries including Nigeria. Local studies have reported a prevalence of about 8-13% (Lawson *et al.*, 2010; Lawson *et al.*, 2011). Perceptibly, this could pose danger to the control of tuberculosis and outcomes of treatments among women with TB and HIV co-infections. It is thus important for health-care workers to routinely make enquiries about adherence from clients as well as monitor adherence indicators such as drug pick-ups and pill counts.

In conclusion, HIV infections and tuberculosis co-existence was recognised among pregnant women in some health facilities in South-western Nigeria. With routine TB screening in antenatal clinics and proper management of cases, a high cure rate is feasible. Sustained strategies against TB- HIV co-infection cannot be over-emphasised. Such strategies include routine TB screening in antenatal clinics, a high index of suspicion for TB among HIV positive pregnant women and proper management of cases according to the national guidelines. Appreciable collaboration and advocate for strong political will for HIV and TB control programmes to sustain cure rates should thus be sustained.

ACKNOWLEDGEMENT

The authors would like to express their sincere gratitude to all authorities, research assistants; and health care workers who have contributed to making this study possible.

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