

## **IMPROVING MATERNAL HEALTH IN THE FACE OF TUBERCULOSIS: THE BURDEN AND CHALLENGES IN ILE-IFE, NIGERIA.**

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### **ABSTRACT**

**Context:** The super-imposition of tuberculosis on the demands of pregnancy confers a grim prognosis.

**Objectives:** To determine the prevalence, pattern of presentation, management and outcome of tuberculosis among pregnant women in Ile-Ife during the first 10 years of the Millennium Development Goal-driven intervention.

**Study Design:** A retrospective analysis of 29 women managed for tuberculosis during pregnancy and the puerperium at the Obafemi Awolowo University Teaching Hospitals Complex (OAUTHC), Ile-Ife between 2001 and 2010 was done using SPSS version 16.0. Prevalence was determined using the total deliveries over the same period. Social class was determined using the Olusanya et al classification and assessment for congenital tuberculosis was done with Cantwell's diagnostic criteria.

**Results:** There were 29 women with tuberculosis in pregnancy and puerperium, with 15,194 deliveries during the review period; giving a prevalence of 191 cases/100,000 deliveries. Cough and weight loss were the commonest complaints, and 53% of screened subjects were retroviral positive. Only 24% of these women were successfully treated using Directly Observed Treatment Short course; strike action and financial constraints being the hindering factors in 36% of them. The mean weight and EGA at birth were 1.87±0.69kg and 35.1±4.0 weeks respectively. Maternal and fetal case-fatality rates were 16.6% and 31.6% respectively.

**Conclusion:** The high prevalence of tuberculosis in pregnancy in Ile-Ife is comparable to the national

figures. The associated high fetomaternal morbidity and mortality rates also contribute to the unhealthy statistics of the country. Prevention of HIV infection and consistent health service delivery are advocated to reduce this scourge.

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## **INTRODUCTION**

Globally, an estimated 287,000 maternal deaths occurred in 2010. About 56% of these deaths occurred in Sub-Saharan Africa; with Nigeria alone contributing about 14% of the global burden. Tuberculosis (TB) is a significant contributor to this alarming rate of maternal mortality in Africa, being one of the **three leading causes of death among women** aged 15-44 years. About 320,000 women were reported to have died from tuberculosis in 2010, and the disease was declared second only to HIV/AIDS as the leading cause of death due to a single infectious disease in 2011. Two TB-high burden countries; India (19%) and Nigeria (14%) contributed a third of the total global burden of maternal deaths recorded in 2010.

This recognizable interplay between tuberculosis and maternal mortality easily justifies the renewed efforts currently being directed at tuberculosis prevention and control. The specific mention of TB among the diseases targeted by the United Nations Millennium Development Goals (UN MDG 6; target 6C) further brought the disease under the global spotlight. Gaps have however remained in the availability of vital information on the current impact of tuberculosis in Nigeria after more than 10 years of MDG-driven interventions. We therefore set out to assess the prevalence and impact of tuberculosis on the course and outcome of pregnancies managed at the Obafemi Awolowo University Teaching Hospitals Complex, (OAUTHC) Ile-Ife, Nigeria during the first 10 years of the UN MDG programme. Our study also aimed to identify the significant factors affecting the management of these patients in our setting.

## **SUBJECTS, MATERIALS AND METHODS**

The study was conducted at the Obafemi Awolowo University Teaching Hospitals Complex, a tertiary health centre located in Ile-Ife, a semi-urban town in Osun State, South-west Nigeria. The major occupations of the inhabitants include farming, public service, craftsmanship and trading. The population is multiethnic, consisting mainly of Yoruba, Ibo and Hausa.

The Health Information Service Department of the hospital was consulted and all the patients with tuberculosis in pregnancy and puerperium that were managed at the Obafemi Awolowo University Teaching Hospitals Complex, Ile-Ife between January 2001 and December 2010 were identified. Information related to the bio-demography, clinical presentation, treatment, complications and feto-maternal outcome were obtained from the case notes using an appropriately designed study proforma. The records of yearly births during the period under review were obtained from the Hospital Statistics Department. Social class was determined using the Olusanya et al classification and assessment for congenital tuberculosis was done with the Cantwell's diagnostic criteria. The resulting data was analyzed using SPSS version 16.0.

## **RESULTS**

Between January 2001 and December 2010, 29 women were diagnosed with tuberculosis during pregnancy and the puerperium, and there were 15,194 deliveries in OAUTHC, Ile-Ife; giving a prevalence of 191 per 100,000 deliveries. Some vital information were missing from the case records of four of the patients. Further analysis was therefore based on the 25

patients (94.8%) with adequate records.

The mean age of the patients was  $27\pm 6.5$  years, with a range of 19 to 43 years. Their parity ranged from 0 to 8, with a median of 2. Only 20 of these patients had sufficient information to be classified into social classes, and 17 (85%) of them belonged to social class 5. Twenty-one (84%) of these patients did not receive antenatal care in the pregnancy prior to the diagnosis of TB. The diagnosis was made in the first trimester in only three of the 17 patients that were diagnosed in the antenatal period, while seven patients each were diagnosed in the second and third trimesters. The remaining eight patients presented in the puerperium.

The commonest presenting complaints were cough and weight loss. Eight (53%) of the 15 patients whose retroviral screening results were available tested positive. The presenting complaints were however similar between the HIV positive patients and their negative counterparts (table 1).

Twenty (80%) of the patients had pulmonary tuberculosis, while extra-pulmonary involvement was present in five of them, including tuberculosis of the spine in four patients (16%), and tuberculous meningitis in one patient (4%). TB was correctly diagnosed at presentation in 18 (72%) of the patients based on clinical symptoms and signs while another five (20%) were initially misdiagnosed as pneumonia in pregnancy.

All the patients were admitted for investigation and treatment, with total duration of stay on admission ranging between four and 59 days. The mean duration of stay on admission was  $25\pm 16.2$  days. Anti-tuberculous therapy was commenced in 22 (88%) of the 25 patients; the commonest indication for instituting treatment

being abnormal findings on roentgenography in 13 (52%) of them. Ziehl Neelsen staining of sputum for acid fast bacilli was positive in only five (20%) of these patients while another four (16%) had a therapeutic trial. Directly Observed Therapy, Short Course (DOTS) was utilized in all 22 patients treated; rifampicin, isoniazid, pyrazinamide and ethambutol being the commonest combination. The Respiratory Unit was involved in the co-management of 22 (88%) of the 25 patients; other units included Neurology (16%), Orthopaedics (16%), Haematology (12%), Cardiothoracic unit (16%) and Psychiatry (4%). None of the patients developed adverse drug reaction and none of the newborns exposed to anti-Koch's treatment in utero had any anomaly at birth. There was none of the neonates with features suggestive of congenital tuberculosis.

Nineteen (76%) of these patients had clinically-evident wasting at presentation. Other medical complications included anaemia, severe enough to warrant blood transfusion in nine women (36%), and pleural effusion that required closed thoracostomy tube drainage in four (16%) of them. Intra-uterine growth restriction was suspected in six (35%) of the 17 patients diagnosed antepartum. Twelve (75%) of the 16 babies whose birth weights were known had low birth weight (with mean birth weight of  $1.87\pm 0.69$ kg), while seven (43.7%) of these deliveries occurred prematurely. The mean gestational age at delivery was  $35.1\pm 4$  weeks. A peculiar complication was the development of 3<sup>rd</sup> degree uterovaginal prolapse in one of the patients in the postpartum period following several bouts of cough.

The Anti-tuberculous treatment schedule was completed in only six (24%) of the 25 patients, while more than a quarter of these patients (28%)

were lost to follow-up as shown on table 2.

Three maternal deaths were recorded among the 18 patients whose outcome as at time of discharge from the hospital was known, with a maternal case-fatality rate of 16.6%. Two of these three patients were diagnosed with TB in the third trimester, while the third was diagnosed in the puerperium. These three patients were unbooked and they all had extra-pulmonary involvement. Six of the 19 patients whose information on perinatal outcome were available had perinatal death; giving a perinatal case-fatality rate of 31.6%. There were concurrent maternal and perinatal losses in two patients.

## **DISCUSSION**

The prevalence of 191 per 100,000 deliveries reported for tuberculosis in pregnancy and puerperium in this study is comparable to the 199 per 100,000 reported for the general population of Nigeria in 2011 by WHO. This further confirms the assertion that the prevalence of tuberculosis in pregnancy is expected to be similar to that in the general population of that geographical region. The age range of 19-43 years in this study, and the predominance of the low socioeconomic class further lend credence to the ability of TB to perpetuate poverty by affecting the work force of the population. Though, the utilization of antenatal care services in Nigeria is low, the 16% utilization rate recorded among these patients is much less than the 45-58% reported in Nigeria in 2010.

The manifestations of TB in early pregnancy are often confused with early pregnancy symptoms, and the associated weight loss is often masked by the weight gain of pregnancy, thereby making

the diagnosis of tuberculosis in pregnancy more challenging. This may probably explain why only three of the patients in our series presented in the first trimester. Majority of the patients in our series were however accurately diagnosed at presentation based on their florid clinical features. Extra-pulmonary TB was not as common as pulmonary TB in pregnancy in this study, contrary to a UK report where both had similar prevalence.

Tuberculosis in pregnancy is not an indication for admission; the 100% admission rate in our patients was however dictated by the need for initial resuscitation, due to their poor clinical states at presentation. One out of every four patients with TB in this review was initially misdiagnosed as community acquired pneumonia. This highlights the need for a high index of suspicion at all times if the correct diagnosis of tuberculosis is not to be missed.

The unholy relationship between TB and HIV/AIDS was further demonstrated, as more than half of the patients whose retroviral status was known were positive. Though, this is not the practice in our centre, routine screening for TB has been advocated in Prevention of Maternal to Child Transmission of HIV (PMTCT) clinics because of the strong association that has been observed between these two diseases in other studies.

As demonstrated in our review, with appropriate shielding of the fetus, roentgenography is cheap and invaluable in the management of these patients. The tendency to delay x-rays in pregnant women due to concerns about the possible hazards of ionizing radiation to the fetus can only delay diagnosis and institution of proper treatment in low resource settings. The 20% smear positive rate reported in this study is

lower than the 58% reported for the country in 2010, possibly due to the inability of pregnant women to generate adequate expulsive force to expectorate the tubercle bacilli.

Interferon gamma assay is a promising investigation that is available in our centre for patients with TB, although its widespread use is presently limited by cost and the inability of the test to differentiate latent from active disease. The Xpert MTB/RIF is a WHO-endorsed rapid molecular test that accurately diagnoses TB and multi-drug resistant TB in 100 minute and is now available at a concessional price to about 145 countries globally. This is expected to facilitate early diagnosis and accelerate patient's access to appropriate care.

Globally, low birth weight affects some 20.6 million babies annually, and its 96.5% predominance in developing countries is a reflection of the maternal health status in these countries. The 75% case-related prevalence of low birth weight in our review is however about 5 times the average global prevalence of 15.5%. Tuberculosis is associated with a high prevalence of growth restriction in utero and preterm delivery.

Directly Observed Treatment using the Short Course strategy (DOTS) is the practice in our Centre, and the anti-tuberculous drugs are available at no cost to the patients.

However, the 100% admission rate and the need for other supportive therapy including investigations, blood transfusion, antibiotics and intravenous infusions for which patients usually have to make out of pocket payments probably explain the 28% rate of discharge against medical advice on financial grounds. Additional efforts at making their

investigations and other supportive treatment available at no extra cost as we currently do for retroviral positive patients will definitely improve the outlook for these patients.

Another 28% of our patients in this review were lost to follow-up after an initial stabilization and commencement of treatment, perhaps due to the paradoxical relationship between feeling of wellness and compliance with treatment in patients with chronic diseases. This act results in the development of multi-drug resistant TB and must be discouraged by ensuring adequate counselling on drug compliance, and a devoted community-health system partnership programme.

The high maternal and perinatal case-fatality rates in our review underscores the devastating effect of tuberculosis on fetomaternal health in Nigeria, and the situation may not be too different in other developing countries where the disease is prevalent. As a further boost to UN MDG 6C, the Global plan to stop TB initiative was launched in 2006, with the aim of reducing the prevalence and mortality of TB by 50% in 2015 and eradicating TB by 2050. These targets are currently expected to be met by all regions globally except the African sub-region where Nigeria belongs. Eradication of TB will improve the chances of achieving the overall targets of the MDGs by contributing to improvement in maternal and child health, as well as reducing poverty. Morbidity and mortality among people living with HIV, 25% of which is directly attributable to TB will also reduce remarkably if this strategy is adopted.

The current statistics of Nigeria demands additional strategy and improved co-ordination to achieve the desired goals on tuberculosis. While millions of patients have been treated and

cured of their disease since the introduction of DOTS, it is essential to state that chemotherapy is only a necessary, but insufficient approach to the eradication of tuberculosis. The other components of DOTS, including political will, at least 70% case detection rate through microscopy, adequate treatment of cases and impeccable record keeping must be emphasized as well.

The establishment of a reliable community surveillance system will facilitate the detection of tuberculosis better than the current hospital-based approach, and reduce the non-compliance rate among our patients, thereby reducing the incidence of multi-drug resistant TB. The collaborative community-based surveillance system established by the Federal Ministry of Health of Nigeria and the World Health Organization is a right step in this direction. We must also ensure meticulous civil data registration and disease notification, as these are complementary to a functional surveillance system in providing essential data for national planning.

HIV/AIDS has especially devastating effects in developing countries, and the nationwide fluctuations in the prevalence of TB are HIV-driven. Investments in awareness programmes and other measure to prevent HIV infection will therefore ultimately reduce the prevalence of TB. Isoniazide preventive therapy (IPT) for tuberculosis is a WHO innovation that is aimed at preventing tuberculosis among HIV positive individuals by the administering Isoniazide at predetermined intervals; caution is however advised as WHO is yet to provide recommendations on the specific dose and time of administration during pregnancy.

Consistent health-service delivery is inevitable in tuberculosis eradication programmes. This

should include accessible antenatal care services, and improved access to free investigations and treatment of HIV and TB. The Xpert MTB/RIF test is now available for routine use in 26 of the 145 countries that were granted concessional prices but Nigeria is yet to avail itself of this opportunity. Health-related human resources must also be optimized and the urban-rural dissociation in health service delivery in Nigeria must be appropriately addressed.

Nigeria currently ranks 10<sup>th</sup> of the 22 TB-high burden countries, and our annual maternal mortality reduction rate of 2.6%, which is barely half of the expected UN MDG 5 annual target of 5.5%, is not satisfactory either. Eradication of poverty and improvement in the standards of living are advocated as worthy investments to reduce this scourge. While collaboration with international donor agencies and non-governmental organizations is in line with UN MDG8, it can only be expected that the Nigerian Government will take up the responsibility of committing adequate human and financial resources to the health of its citizen, without having to rely on these support.

#### **ACKNOWLEDGEMENT**

The authors hereby declare no acknowledgement.

#### **CONFLICT OF INTEREST**

All the authors hereby declare no conflict of interest.

**Table 1:** Presenting complaints of patients with tuberculosis in pregnancy and puerperium in Ile-Ife, Nigeria.

Presenting Complaint	Retroviral Status			Total (n=25)
	Positive (n=8)	Negative (n=7)	Not Available (n=10)	
Cough	6	6	7	19
Weight loss	4	6	7	17
Night sweat	4	3	3	10
Evening pyrexia	3	3	4	10
Paraplegia	2	2	1	5
Haemoptysis	2	2	1	5

**Table II:** Outcome of treatment of patients with tuberculosis in pregnancy and the puerperium in Ile-Ife, Nigeria.

Treatment outcome	Frequency (%)
Treatment completed	6 (24)
Lost to follow -up	7 (28)
Discharged against medical advice	7 (28)
Referred during strike action	2 (8)
Dead	3 (12)
Total	25 (100)

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