

PULMONARY TUBERCULOSIS AMONG PREGNANT MOTHERS IN TANZANIA

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ABSTRACT

OBJECTIVES

Determining the prevalence of Pulmonary Tuberculosis (PTB) during pregnancy in Northern Tanzania.

DESIGN

In a prospective cross-sectional study.

RESULTS

Latent Tuberculosis Infection (LTBI) was detected in 86 out of 287 pregnant women (29.9%). Active PTB was diagnosed radiologically in four subjects (1.4%). All cases were sputum smear-negative

CONCLUSION

LTBI and subsequently active PTB is a public health problem among pregnant mothers in Northern Tanzania.

INTRODUCTION

It is estimated that TB infection is present in one-third of the world's population, or two billion people. Eight million new cases of active disease have been estimated to occur worldwide annually.¹ Currently, more than 3 million people die from tuberculosis every year. The greatest burden of latent TB infection is found in Southeast Asia (prevalence, 46%), the Western Pacific region (32%), Africa (31%), and the Eastern Mediterranean region (27%).²

Women between the ages of 15 and 49 years carry the greatest risk of converting from tuberculosis infection to the disease.³ It is expected that the incidence of tuberculosis among pregnant women would be as high as in general population. In a South African study, TB was the third leading cause of maternal mortality, mostly in combination with HIV-infection.⁴ Neonatal mortality and extreme prematurity have also increased significantly due to the problem.⁵ Tanzania has not been spared.⁶ In spite of these high figures, reports of this combined infection in pregnancy have been sparse.⁷

The study was aimed at determining the prevalence of PTB in pregnancy and co-infection with HIV in Tanzania.

METHODOLOGY

Settings

An urban hospital based cross-sectional study was undertaken at the Ngarenaro and Levelosi clinics. These are resource poor settings with minimal microbiological lab support. The study population included all consenting pregnant women attending clinic during a total study duration of 4 weeks, with an intention to treat. Allowing for a 20% failure to follow up, a minimum sample size of 395 was reached. Ethical clearance was obtained from the MUHAS community health department and the National Tuberculosis and Leprosy Program.

Screening Methods

Eligible participants in our study were subjected to a TB symptom check-list followed by a thorough physical examination. They were also subjected to the Mantoux test which involved injection of 0.1 ml of PPD (Purified Protein Derivative) RT 23 SSI intradermally using standard procedures. Results were interpreted 48 hours later using the ball-point pen method⁸ and proof read by a senior researcher. Those with a productive cough or cough for at least 2 weeks had

their “spot” and “morning” sputum screened for Acid Fast Bacilli (AFB).

Sputum specimens were dissolved in an equal volume of household bleach (5% Sodium Hypochlorite), then left for 10 minutes at room temperature (25° C) with vigorous shaking at regular intervals. This was followed by addition of 8 ml of distilled water after which the suspension was centrifuged at 3000 g's for a further 10 min. The supernatant was carefully poured off, and the sediment stained using Ziehl Nielsen's technique. This centrifugation technique has been shown to be superior to direct microscopy as far Acid fast bacterial yield (sensitivity) is concerned.⁹ The slides were interpreted by two independent laboratory technicians in a blinded fashion.

All those with productive cough, cough lasting more than two weeks or a positive Tuberculin Skin Test (TST) were subjected to a single postero-anterior chest radiograph (CXR) with abdominal shielding. The CXRs were interpreted by two independent radiologists in a blinded fashion. Pregnant mothers found to be having Active Pulmonary Tuberculosis were counselled and referred to a TB centre for treatment and follow-up.

Data processing and analysis

The data was processed using the Epi-Info v.6 statistical package. Fischer's exact p-values, Chi-squares, regression analyses and Odd's ratios were calculated. A Fisher's exact 2-tailed P-value of less than 0.05 was considered significant. Scatter plots were utilized in the detection of trends and patterns.

Inclusion criteria

Pregnant women with gestational ages from 12 weeks to full term were included in the study.

RESULTS

Of the 396 women initially screened, 287 (72.5%) returned to have their Tuberculin Skin Tests (TSTs) read. The mean age of those screened was 24.9 years, ranging from 16 to 40 years. The mean Body Mass Index for this subpopulation stood at 25.06 kg/m². (95% CI=24.6 – 25.5 kg/m²)

The mean TST induration in those with a positive result was 19.4 mm (95% CI 18.2 – 20.5 mm). A positive TST result was defined as at least 10mm induration for HIV

negative patients and 5 mm for HIV positive ones.

Table 1: Prevalence of Latent TB infection, Active PTB and HIV among pregnant women attending ANC

TST INTERPRETATION (LTBI)	Frequency	Percent
POSITIVE	86	29.9%
NEGATIVE	201	70.1%
TOTAL	287	100.0%
PTB (Dx by CXR)	Frequency	Percent
NO	283	96.6%
OLD	6	2.0%
ACTIVE	4	1.4%
TOTAL	293	100.0%
HIV sero status	Frequency	Percent
Positive	20	5.1%
Negative	376	94.9%
TOTAL	396	100.0%

A weak positive trend ($P>0.05$) of increasing proportion of positive TSTs with age was noticed which was more pronounced after the age of 30. No significant correlation was observed between LTBI(latent TB infection) and marital status, parity or gestational age. HIV infection influenced TST conversion inversely; the TST positive rate among HIV positive women (23.1%) being lower than that of their HIV negative counterparts (30.3%)

A history positive for 'other contact' of open PTB in the previous two years appeared to confer an increased risk for developing lesions suggestive of active PTB on CXR (OR=16.0; 95% CI(1.5,175.6); $P<0.05$). 'Other contact' referred to one outside the nuclear family but limited to the immediate neighborhood or workplace – it included extended family .When statistical analysis for the combined risk conferred by “family” AND/OR “other” TB contacts was carried out, the following results were obtained: Odd's Ratio= 8.6; 95% CI (0.8 <OR< 89.9); $P=0.06$.

Of the symptoms reported by pregnant women in our study the most common were malaise (36.6%), loss of appetite (19.2%), pleurisy (14.1%) and fever (13.1%) (Table 2). Most (88.4%) women had no abnormalities on percussion or auscultation. Among the four active PTB subjects, anomalies detected on examination included a pleural

effusion and rhonchi in one (1) case each. The latter feature i.e. rhonchi was reported in an HIV/PTB co-infected subject. Only two symptoms showed a strong positive correlation with a chest X-ray diagnosis of active PTB. These were cough for more than two weeks (OR=63.7; 95% CI (5.2, 1741.7); $P<0.01$) and productive cough (OR=42.6; 95% CI (3.6, 1138.9); $P<0.01$). One (25%) of the four active PTB cases diagnosed was completely asymptomatic.

Table 2: Frequency distribution of clinical features suggestive of PTB among all pregnant women:

Clinical features (symptoms)	Frequency	Percent (of 396)
Malaise	145	36.6%
Loss of Appetite	76	19.2%
Pleurisy	56	14.1%
Fever	52	13.1%
Dyspnoea	33	8.3%
Weight Loss	30	7.6%
Productive Cough	26	6.6%
Cough > 2 weeks	20	5.1%
Night Sweats	18	4.5%
Haemoptysis	1	0.3%
Clear	350	88.4%
Rhonchi	21	5.3%
Crackles	16	4.0%
Bronchial breath sounds	8	2.0%
Pleural rub	1	0.3%
Pleural effusion	1	0.3%

Radiologic changes consistent with a diagnosis of active PTB were present in a total of four patients, two of whom were HIV co-infected. Radiologic findings which were significantly associated with active PTB included hilar shadowing (OR 30.3, 95% CI 2.37-852.4, $P<0.01$); cavitation especially apical (OR=110; 95% CI 4.6-5714, $P<0.01$), pleural effusion, atelectasis and hilar lymphadenopathy (all with OR undefined, $P<0.05$).

Out of 28 subjects whose sputum was obtained for examination, no AFB positive smears were detected. Hence all cases diagnosed based on chest radiography were smear negative for Pulmonary tuberculosis.

DISCUSSION

The prevalence of Latent tuberculosis infection (LTBI) among pregnant women in this study was 29.9% and does not differ significantly from that of other African countries (31%).¹¹ Acquisition of TB infection is highest during reproductive age and pregnancy does not alter the immunological reactivity to tuberculin as indicated in several studies.^{12, 13} Active PTB in this population (1.4%) is quite prevalent considering the range of 0.1%-1.9% derived by two independent researchers, Hamadeh and Tran JH.^{14,15} This is worrying considering the fact that in Sub-Saharan Africa, TB is becoming an increasingly important cause of non-obstetric mortality⁴ and adverse pregnancy outcomes.¹⁶ According to the Tanzania Demographic and Health Survey (TDHS) 2004/05, the prevalence of pregnancy among a subpopulation of 15-49 year old females was 10.5%. Considering the active PTB prevalence from our study 1.4% gives an alarming estimate of 12,121 cases of active PTB in pregnancy, nationwide, at any given point in time.¹⁷ Furthermore, the risk of mother-to-child-transmission for active disease is 15% within 3 weeks of delivery.¹⁸

The relationship between age and TST results may be the effect of cumulative exposure to *M. tuberculosis* over several years, since an individual's risk of exposure is a product of concentration of infected droplets in the air and the length of time a person breathes that air.²¹ We found that parity had no significant influence on the incidence of PTB, a finding echoed by a South African study which revealed no significant difference between those pregnant women diagnosed with PTB and those who were not as far as age and parity were concerned. ($P=0.9$, 0.8 respectively).⁴

No cases of active PTB had a history of 'family contact' in our study, but half of the diagnosed active PTB cases had a history of 'other contact' exposure within the preceeding two years (OR =16.0, $P<0.05$). These results are similar to those in conducted among a study in Iraqi children, which showed that those living in extended families had a higher TB infection rate compared to those living within nuclear families ($r=0.72$, $P<0.05$).²²

Previous studies including a prominent one published by Centre for Disease Control, Atlanta have reported that HIV positive subjects are less likely to be

TST-positive than HIV-negative ones; something that we also noted.²³ This is likely due to the defective cell-mediated immune response in this high risk group which is necessary for delayed type hypersensitivity, the basis of the tuberculin skin test. Another limitation of tuberculin skin testing brought to light in our study was its low Positive Predictive Value (2.4%) for active PTB making it economically and logistically unsuitable for mass screening. This is the reason why many authorities now recommend its use be limited to screening among high risk individuals, chiefly consisting of patients suffering from immunosuppression and chronic debilitating diseases.^{24,25}

The two most common symptoms reported by pregnant women in our study were malaise 36.6% and loss of appetite 19.2% and other symptoms including dyspnoea (8.3%) were likely due to the physiological changes of pregnancy itself, which often mimic the earlier constitutional symptoms of PTB.²⁹ The most common symptoms reported in a South-African study by Kali et al were malaise, cough, productive cough and shortness of breath.²⁶ As far as HIV positive pregnant women are concerned; the occurrence of constitutional symptoms further increases the diagnostic difficulty as they can be caused by HIV infection itself.

Radiology is highly sensitive for PTB as demonstrated by Good et al in whose study all the 27 pregnancies diagnosed with culture positive PTB had abnormal CXRs²⁷, this can further be improved when combined with symptom screening. The CXR findings reported in the cases of active PTB without HIV co-infection were hilar shadows and apical cavitation (both cases), right sided pleural effusion and infiltrates in the mid and upper zones (one case). HIV positive subjects with active PTB had atypical patterns on CXR: one case had infiltrates in the Left upper zone with atelectasis as shown by elevation of the left hemi diaphragm. One of the patient had been treated for PTB three years prior to our study, but was showing clinical features of disease reactivation which was confirmed radiologically. Another co-infected case had micro nodules (>3mm) in the lower zone and hilar lymph node enlargement with calcification. No cavitation or pleural effusions were noticed in the HIV positive group. In the later stages of HIV infection, the CXR appearance of active PTB resembles that of primary

TB often with infiltrates rather than cavities. Also, the lower zones are more likely to be involved than the upper ones.

Our study revealed two symptoms having a positive correlation with CXR diagnosis of PTB: cough for more than two weeks (Odd's ratio (OR) 63.7) and productive cough (OR, 42.6). One of the four women diagnosed with active PTB in our study was asymptomatic. Comparing our study with that of Kali et al, clinical features appearing with similar frequencies in both studies included cough (75% vs. 74%), fever (25% vs. 30%) and asymptomatic (25% vs. 20%). On chest examination, abnormalities were detected in only two of the four active PTB cases, pleural effusion in one case and scattered rhonchi over the posterior upper thorax in the other. It is known that the physical exam in PTB may reveal scattered rhonchi and wheezes,¹⁸ however a history of atopy is usually against a diagnosis of PTB. In fact, a finding of crackles actually decreases the likelihood of a CXR diagnosis of PTB.¹⁰

All sputum smears in our study were AFB negative; a factor associated with lower risk of mother-to-child transmission (MTCT) of TB. Our findings are not isolated since a study at Rhodes island, 1993, showed pregnant women with pulmonary conditions were more likely to present with unilateral non-cavitary, smear-negative disease ($p=0.02$)²⁸ Similarly, Kali et al in a South African study, found that all eight pregnant women diagnosed with active PTB were sputum AFB negative but culture positive.²⁶

The risk score derived in this study is of particular value in pregnant women situated in low resource settings since it uses no lab/radiographic parameters. As compared to the risk score derived by Wisnivesky, it has a higher PPV (Positive Predictive Value) and Specificity, but a lower Sensitivity. Our risk score may also be useful as a tool for excluding active PTB before initiation of Isoniazid prophylactic therapy (IPT) and for screening HIV positive candidates prior to vaccination with the newly developed *M.vaccae* vaccine.²⁹ In any case, well structured case control studies are required to verify its statistical significance.

CONCLUSION

The prevalence of latent TB, active PTB and co infection with HIV among pregnant women in Tanzania is relatively high with direct implications on the incidence of neonatal tuberculosis. These findings necessitate more serious thought on the issue of targeted TB screening during pregnancy keeping in mind the consequences of late diagnosis, the non-specific presentation of the disease during pregnancy and the specific needs and vulnerabilities of both mother and fetus. Once found to have a positive TST

in the absence of laboratory radiographic evidence for active disease, the issue of using Isoniazid Prophylactic Therapy (IPT) comes to surface and needs to be clearly addressed in standard guidelines.

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