International Journal of Clinical Obstetrics and Gynaecology

ISSN (P): 2522-6614
ISSN (E): 2522-6622

www.gynaecologyjournal.com
2021; 5(1): 347-351
Received: 13-10-2020
Accepted: 25-11-2020

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A comparative study of maternal and perinatal outcome in primary pulmonary tuberculosis in pregnancy in a tertiary care institute

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DOI: https://doi.org/10.33545/gynae.2021.v5.i1f.836

Abstract
Aims and objectives: Early diagnosis and treatment of tuberculosis in pregnancy and to understand the maternal and perinatal outcome.
Materials and methods: The present prospective case control study was conducted in the outpatient and inpatient unit of department of Obstetrics and Gynecology Lokmanya Tilak Municipal Medical College and Hospital, Mumbai. Cases: Pregnant women's attending Antenatal care OPD or IPD who were already on Anti- tuberculosis treatment (ATT). Controls: Health pregnant women attending ANC OPD or IPD.
Maternal outcome: Antenatal Hospitalization /Miscarriages/Suboptimal Weight Gain in Pregnancy/Maternal Morbidity and Mortality. Perinatal outcome: Low birth weight (LBW) /Intrauterine Growth Restriction (IUGR) / Small for Gestational Age (SGA) babies /Prematurity/Congenital anomalies.
Results: The mean age of the women in the case and control groups were 24.52 years (range being 24 to 28 years) and 25.42 respectively. 89% of the active tuberculosis cases were anemic when compared with the healthy controls. 8% of active tuberculosis pregnant mothers had abortion. 27% of active tuberculosis pregnant mothers had intra uterine growth restriction when compared with the healthy controls.
Conclusion: Early diagnosis is therefore a major step in the prevention of adverse outcome of tuberculosis in pregnancy. Screening of tuberculosis should be motivated even in the absence of overt signs of the diseases.

Keywords: Tuberculosis, pregnancy, IUGR, anemia, abortion

Introduction
Tuberculosis is the leading cause of disability and death in developing countries especially in Asian and Sub –African regions. Despite a decrease in the incidence of tuberculosis by the tremendous effort by the International and National organizations, tuberculosis disproportionally affects the women of reproductive age group [1]. Globally, an estimate of 900 million of women with Latent Mycobacterial Tuberculosis Infection (LTBI) especially the pregnant women were more likely to develop into active tuberculosis when compared to the non-pregnant women. It is also observed that pregnant women rapidly develop active tuberculosis and acquire new infection when compared to the non-pregnant women [2].
The high delirious effect of tuberculosis on pregnancy could be explained due to hormonal, immunological and physiological changes during pregnancy which provide an opportunity for infection or re-infection. Due to suppression of T-helper 1(Th1) proinflammatory response during pregnancy, the women may not present with typical symptoms which may lead to the late diagnosis and treatment [3]. World Health Organization estimates that 3 million active tuberculosis cases are missed annually and therefore it insists active case finding during pregnancy. 1 Also the tuberculosis in pregnancy follows a vicious cycle of poverty, under nutrition, delayed diagnosis, irregular treatment and follow up in developing countries [4].
In 2014, WHO estimates that 3.3 million women have active tuberculosis and leading to a mortality of 5, 10,000. Among the non –obstetric causes maternal mortality tuberculosis tops the most. 40% of deaths in pregnancy are due to untreated tuberculosis [1]. In Africa, 47% causes of maternal death are due to non-obstetric causes like meningitis, tuberculosis and pneumonia. The data regarding the prevalence of tuberculosis in pregnancy in India is scarce due to variability in the observed maternal outcome in the pregnancy. It is estimated that tuberculosis accounts 2.3 per 1000 pregnant women which is approximately 44,500 patients annually [5].

The pregnant women with Tuberculosis have unfavorable maternal and fetal outcomes, which includes six fold risk in perinatal deaths and 2 fold risk in preterm deaths and low birth weight [6]. Compared with pregnant without TB, active tuberculosis is associated with increased odds of caesarean delivery, preterm birth, low birth weight, birth asphyxia and perinatal death. This maternal and perinatal outcomes occurs 25% in pregnancy and 16% in perinatal period in total person-time [7]. Considering the high burden of tuberculosis in pregnancy and perinatal period, effective screening tool like sputum smear examinations should be done during antenatal period to facilitate the early diagnosis and treatment [8]. Hence the present study was conducted was done for early diagnosis and treatment of tuberculosis in pregnancy and to understand the maternal and perinatal outcome and to take prompt management for its prevention in a tertiary care teaching hospital.

Material and Methods

The present prospective case control study was conducted in the outpatient and inpatient unit of department of Obstetrics and Gynecology Lokmanya Tilak Municipal Medical College and Hospital, Mumbai, for a period of 18 months

Ethical consideration

Institutional Ethical Committee approval of Lokmanya Tilak Municipal Medical College and Hospital was obtained before starting the study. The participants were explained that the data collected in this study will be used only for research purposes. The participants were explained about the freedom of withdrawal from the study at any time without penalty or loss of benefits. The confidentiality of the data collected from the enrolled participants was maintained in all the phases of the study. The study participants who required medical attention during the period of intervention were referred to the respective departments.

Groups

Cases: Pregnant women's attending Antenatal care OPD or IPD who were already on Anti- tuberculosis treatment (ATT).
Controls: Health pregnant women attending ANC OPD or IPD
Sample size estimation

The formula used

$N= (Z1- \alpha + Z1- \beta)2 \times p \times q$

Considering alpha error for sample size calculation as 0.05 and the power of study as 80%, accounting for the loss to follow up/ non participation the sample size was calculated from the formula was 100 patients in each group.

Inclusion criteria

Cases
Age: 18-45 years
All ANC OPD and IPD patients who are newly diagnosed primary pulmonary tuberculosis or on AKT.

Control

Age-18-45 year's healthy pregnant females without any Obstetric medical/surgical complications No active pulmonary tuberculosis infection No past history of TB or TB contact

Exclusion criteria

Patients not willing to be included in the study Obstetrical Medical/Surgical complications-example: Diabetes Mellitus, PIH, Chronic hypertension, Hydramnios, IUGR, Anemia, Heart disease Past history of tuberculosis with completed AKT course and declared cured/relapse/defaulters.

MDR TB

All HIV-TB co infected cases
Extra pulmonary tuberculosis

Sampling method

Using simple random sampling method the eligible participants was assigned in a 1:1 ratio in case and control group using computer generated random number.

Data collection

The study was started after obtaining Institutional ethical approval. The purpose and procedure of the study was explained to the enrolled participants in their local language. Patient information sheet and informed written consent was obtained from the participants before initiating the study.
Patients attending ANC OPD as well as IPD were evaluated with proper history and examination to identify cases of active pulmonary tuberculosis without any other obstetric medical/surgical complication. Such patients were further subjected to routine investigations including sputum AFB as mentioned above. In a similar manner normal healthy ANC OPD/IPD patients will be screened without active pulmonary tuberculosis or past history of Pulmonary Tuberculosis or TB contact, without other obstetric medical/surgical complications.
Both the groups of pregnant women with/without disease were compared over whole ANC period and maternal and perinatal outcome were derived.
Maternal outcome: Antenatal Hospitalization /Miscarriages/Suboptimal Weight Gain in Pregnancy/Maternal Morbidity and Mortality.
Perinatal outcome: Low birth weight (LBW) /Intrauterine Growth Restriction (IUGR) / Small for Gestational Age (SGA) babies /Prematurity/Congenital anomalies.

Statistical analysis

The collected data was checked for completeness before entering into the Microsoft excel spread sheet. The validation of the data was checked at regular intervals. Data analysis was performed w using Statistical Package for Social Sciences (SPSS IBM) 21. The quantitative data was expressed in mean, standard deviation and proportions. T test and Chi square was applied and p value <0.05 was considered statistically significant. Multivariate analysis was done for strength of association.

Results

Table 1: Distribution of mean age, GA (Date and USG)

Variables	Groups		p-value
	Case	Control	
Age	24.52±4.15	25.42±4.64	0.150
GA (Date)	33.74±7.19	36.85±1.70	0.001*
GA (USG)	34.06±7.40	37.09±1.81	0.001*

Table 2: Distribution of study subjects according to parity and mode of delivery

Variables		Groups		p-value
		Case N=100	Control N=100	
Parity	Primigravida	33 (33%)	39 (39%)	0.377
	Multigarvida	67 (67%)	61 (61%)	
Mode of Delivery	Cesarean section	20 (20%)	28 (28%)	0.317
	Normal	72 (72%)	72 (72%)	
	Abortion	8 (8%)	(0%)	
Total				

Test applied: chi-square test

Table 3: Distribution of study subjects according to type of delivery

Variables	Groups		p-value
	Case N=100	Control N==100	
Abortion	8 (8%)	0 (0%)	0.001*
Pre-term	37 (37%)	23 (23%)	
Term	55 (55%)	77 (77%)	

Test applied: chi-square test

Table 4: Distribution of anemia, birth weight, IUGR and NICU

Variables	Groups		p-value
	Case N=100	Control N=100	
Anemia	89 (89%)	70 (70%)	0.001*
IUGR	27 (27%)	0 (0%)	0.001*
Low Birth Weight	57 (57%)	18 (18%)	0.001*
NICU Admission	26	6	0.001*

Test applied: chi-square test

Discussion

Tuberculosis disease is as old as human history. 75% of people affected with tuberculosis are in the economically productive age group [1]. This proportionally affects the socioeconomic development and increases the poverty cycle. Due to confounding factors, the exact of incidence of tuberculosis in pregnancy is not available and tuberculosis is the third leading cause of death among the women's of reproductive age group in the developing countries [9].

The accurate incidence and progression into active tuberculosis in pregnancy is expected to be much higher than the general population. The challenging fact in tuberculosis in pregnancy is the difficulty in early diagnosis since the symptoms of pregnancy cover the tuberculosis [10]. Tuberculosis in pregnancy contributes to significant maternal mortality and adverse perinatal outcome. Tuberculosis in pregnancy is prone to cause obstetric complications like spontaneous abortions, small for date uterus, preterm labour, low birth weight and increased incidence of neonatal mortality [11]. Hence tuberculosis in pregnancy is considered as a double-edged sword where in one end it significantly contributes to maternal morbidity and mortality and the growth of newborn and in other end the exacerbated effects of pregnancy over the progression of tuberculosis. The prevention of the advert effects of tuberculosis in pregnancy goes beyond early screening of all pregnant women for active tuberculosis even in the absence of overt symptoms of the disease.

A case control study was conducted in a tertiary care teaching hospital to study the adverse maternal and perinatal outcome in pulmonary tuberculosis in pregnancy and to evaluate the effectiveness of early diagnosis and prompt management in tuberculosis in pregnancy in the prevention of maternal and perinatal outcome. The pregnant women who had active tuberculosis and on antituberculous treatment in early trimester were allocated in case groups and those antenatal women without tuberculosis were included in control group and studied.

The mean age of the women in the case and control groups were 24.52 years (range being 24 to 28 years) and 25.42 respectively. Gupta *et al*. reported similar results in maternal tuberculosis where the median age of the mothers where 23years (range being 21-25) years [12]. Study by Knight M *et al*. showed a median age was 30 years (range being 20-45 years). From the reviews of global literature it is suggestive that tuberculosis affects disproportionately in reproductive age groups in the different settings of the world [10-12].

This could be explained from the fact that, poor or non – reporting of tuberculosis in health care settings, stigma, and discrimination, cultural and financial barriers act as major obstacles in diagnosing and treating tuberculosis in women. Tuberculosis predominantly affects the women when they are reproductively and economically active which invariably affects their children and families [13]. In the study of Sgaragli G *et al*, in settings like India apart from the age of incidence of maternal tuberculosis, the preexisting malnutrition, poverty, low socioeconomic status, illiterate, lack of knowledge of the diseases and barriers to the health care affects proportionally the maternal and perinatal outcome in tuberculosis [14].

In the current study, 89% of the active tuberculosis cases were anemic when compared with the healthy controls. The prevalence of anemia among TB patients ranges between 30–94%. It has been shown that anemia is more likely to occur among TB patients compared to healthy controls [15]. In the study by Kamija S *et al*. the commonest cause of anemia of inflammation in pregnancy is tuberculosis which accounts for 95% and 98% of cases and deaths of tuberculosis respectively [16].

The anemia is initially mild and overtime it becomes severe and leading to hypochromic microcytic erythrocytes. The anemia in pregnancy due to chronic disease like tuberculosis could be explained that, (i) host defense mechanism which sequester the iron from the invading pathogens, (ii) Increase in the interleukin (IL-1) which is increased during inflammation like tuberculosis inhibits the erythroid colony-forming units [17]. Broek NR *et al*. study showed mild to moderate anemia due to tuberculosis in pregnancy has increased risk of premature delivery, low birth weight, higher perinatal and infant morbidity and mortality [18].

In the current study, 8% of active tuberculosis pregnant mothers had abortion, Knight M *et al*. [19] study abortion rate was 6.25%, Kothari *et al*. [20] abortion rate was 6.3%. 37% had preterm birth when compared with the healthy controls. Similarly Jana *et al*. showed 2 fold increased risk in preterm birth (22.8%, $p< 0.01$) and six fold increase in perinatal deaths (10.1%, $p< 0.001$) among pregnant mothers with active pulmonary tuberculosis [21]. Figueroa-Damián RA *et al*. reported higher risk of premature delivery (RR 2.1; 95% CI 1–4.3) and perinatal death (RR 3.1; 95% CI 1.6–6) when compared to the healthy controls [22]. Asuquo *et al*. showed a liner relationship between preterm delivery and active pulmonary tuberculosis among the study participants ($p< 0.0001$) [23].

In contrast to the above results, Kothari *et al*. showed good maternal outcomes with no morbidity and mortality and majority of active tuberculosis mother delivered at term and there was no incidence of perinatal morbidity and mortality [20]. In the current study, 62% neonate were low birth weight when compared with neonate of healthy controls. Similarly, Jana *et al*. showed 34.2% of low birth weight neonates ($p< 0.001$) with active pulmonary tuberculosis when compared with the normal gravida of same age, parity and socioeconomic class [21]. Figueroa-Damián R A

et al. study showed two fold risk of birth weight of neonate less than 2500gms (RR 2.2; 95% CI 1.1–4.9) among mothers with active pulmonary tuberculosis [22].

Asuquo *et al*. showed mean birth weight was lower in pulmonary TB than in the extra-pulmonary TB. Multivariate analysis showed that low birth weight was associated with pre-term delivery ($p< 0.001$) [23].

In present study pregnant mothers with active pulmonary tuberculosis had 27% of intra uterine growth restriction when compared with the healthy controls. Hendrix N *et al*. reported most common cause of intrauterine growth restriction in developing countries is tuberculosis which results from direct cytolysis and loss of cell function in various organ systems in the fetus [24].

Verma P showed the incidence of IUGR due to infections especially due to tuberculosis higher in developing countries. Although, the mechanism is not clear but oxidative stress, immunological factors, aryl hydrocarbon receptor and adduct formation are some pathways which are involved in IUGR. The consequence of IUGR involves post-birth complications, perinatal mortality and morbidity [25].

In our study, we have noted that there was no significant difference in mode of delivery between the case and control groups ($P > 0.05$). Similar observations were noted previously by Yadav V *et al*. [26]. Tuberculosis (TB) is a global disease with increase in concern with growing morbidity and mortality after drug resistance and co-infection with HIV. Mother to neonatal transmission of disease is well known. Current recommendations regarding management of newborns of mothers with tuberculosis are variable in different countries and have large gaps in the knowledge and practices. It has been noted in literature that there is significant difference in the mean birth weight between case and control groups, the birth weight being much lower in case group [21, 22, 27].

Though the rate of NICU admission for neonates born to case group has not been well established in literature, in our study its noted that there is a significance difference between the case and control group, ($p=0.0001$).

Above results suggests that the adverse perinatal outcome in active tuberculosis mothers is much lesser when compared with other results reported worldwide. There were no maternal morbidity and mortality reported during the study period which is suggestive that early diagnosis and prompt management of pulmonary tuberculosis in antenatal period by cost effective strategies can condense the adverse maternal and perinatal outcome.

Conclusion

Early diagnosis is therefore a major step in the prevention of adverse outcome of tuberculosis in pregnancy. Screening of tuberculosis should be motivated even in the absence of overt signs of the diseases. Moreover, apart from screening the prevention goes behind this is essentially a disease of poverty. Hence improving the living condition, encouraging good ventilation at households, improvement in nutritional status and seeking health care has another important part in prevention of tuberculosis and its adverse maternal and perinatal outcome.

References

1. World Health Organization. Global tuberculosis control 2016. Geneva, Switzerland: WHO 2016.
2. Deluca A, Chaisson RE, Martinson NA. Intensified case finding for tuberculosis in prevention of mother-to-child transmission programs: A simple and potentially vital addition for maternal and child health. J Acquired Immune Deficiency Syndrome.
3. Good JT, Iseman MD, Davidson PT, Lakshminarayan S, Sahn SA. Tuberculosis in association with pregnancy. Am J Obstet Gynecol 1981;140:492–8.
4. Somma D, Thomas BE, Karim F *et al*. Gender and socio-cultural determinants of TB-related stigma in Bangladesh, India, Malawi and Colombia. Int. J Tuberc Lung Dis 2008;12:856–66.
5. Central Tuberculosis Division, Government of India Technical and operational guidelines for tuberculosis control in India. New Delhi: Ministry of Health & Family Welfare 2016.
6. Pillay T, Khan M, Moodley J *et al*. The increasing burden of tuberculosis in pregnant women, newborns and infants under 6 months of age in Durban, KwaZulu-Natal. S Afr Med J 2001;91:983–7.
7. Toro PL, Schneider KL, Carter RJ, Abrams EJ, El-Sadr WM, Howard AA. Maternal and infant outcomes with concurrent treatment of tuberculosis and HIV infection in pregnant women. J Acquir Immune Defic Syndr 2011;56:e63–7.
8. Sangala WT, Briggs P, Theobald S *et al*. Screening for pulmonary tuberculosis: an acceptable intervention for antenatal care clients and providers? Int. J Tuberc Lung Dis 2006;10:789–794.
9. Schaefer G, Zervoudakis IA, Fuchs FF, David S. Pregnancy and pulmonary tuberculosis. Obstetrics and Gynecology 1975;46(6):706–715.
10. Knight M, Kurinczuk JJ, Nelson-Piercy C. Tuberculosis in pregnancy in the UK. BJOG 2009;116(4):584–588.
11. Vallejo JG, Starke JR. Tuberculosis and pregnancy. Clinics in Chest Medicine 1992;13(4):693–707.
12. Gupta A, Bhosale R, Kinikar A, Gupte N, Bharadwaj R, Kagal A *et al*. Maternal tuberculosis: a risk factor for mother-to-child transmission of human immunodeficiency virus. Journal of Infectious Diseases 2011;203(3):358-62.
13. World Health Organization. Global tuberculosis report 20. Geneva: World Health Organization 2015.
14. Sgaragli G, Frosini M, Human tuberculosis I. Epidemiology, diagnosis and pathogenetic mechanisms. Current medicinal chemistry 2016;23(25):2836-73.
15. Chakrabarti S, George N, Majumder M, Raykar N, Scott S. Identifying sociodemographic, programmatic and dietary drivers of anaemia reduction in pregnant Indian women over 10 years. Public Health Nutr 2018;21(13):2424-33.
16. Phiri KS. Approaches to treating chronic anemia in developing countries. Transfusion Alternatives in Transfusion Medicine 2008;10(2):75-81.
17. Bullarbo M, Barnisin M, Vukas Radulovic N, Mellgren Å. Low Prevalence of Active Tuberculosis among High-Risk Pregnant and Postpartum Women in Sweden: A Retrospective Epidemiological Cohort Study Using and Evaluating TST as Screening Method. Infect Dis Obstet Gynecol 2018, 3153250.
18. Van den Broek NR, Letsky EA. Etiology of anemia in pregnancy in south Malawi. The American journal of clinical nutrition 2000;72(1):247S-56S.
19. Knight M, Kurinczuk JJ, Nelson-Piercy C, Spark P, Brocklehurst P. Tuberculosis in pregnancy in the UK. BJOG: An International Journal of Obstetrics & Gynaecology 2009;116(4):584-8.
20. Kothari A, Mahadevan N, Girling J. Tuberculosis and pregnancy-results of a study in a high prevalence area in

London. European Journal of Obstetrics & Gynecology and Reproductive Biology 2006;126(1):48-55.
21. Jana N, Vasishta K, Jindal SK, Khunnu B, Ghosh K. Perinatal outcome in pregnancies complicated by pulmonary tuberculosis. International Journal of Gynecology & Obstetrics 1994;44(2):119-24.
22. Figueroa-Damián R, Arredondo-García JL. Neonatal outcome of children born to women with tuberculosis. Archives of medical research 2001;32(1):66-9.
23. Asuquo B, Vellore AD, Walters G, Manney S, Mignini L, Kunst H. A case–control study of the risk of adverse perinatal outcomes due to tuberculosis during pregnancy. Journal of Obstetrics and Gynaecology.
24. Hendrix N, Berghella V. Non-placental causes of intrauterine growth restriction. Semin Perinatol 2008;32(3):161–5.
25. Verma P, Chaudhary H. Understanding intrauterine growth restriction (IUGR): a review. Journal of Biomedical Sciences 2015;2(4):31-7. 2012 Oct 1;32(7):635-8.
26. Yadav V, Sharma JB, Kachhawa G, Kulshrestha V, Mahey R, Kumari R *et al*. Obstetrical and perinatal outcome in pregnant women with extrapulmonary tuberculosis. Indian Journal of Tuberculosis 2019;66(1):158-62.
27. Heywood SH, Amoa AB, Mola GL, Klufio CA. A survey of pregnant women with tuberculosis at the Port Moresby General Hospital. Papua New Guinea Medical Journal 1999;42(3/4):63-70.