Observational Study

Impact of tuberculosis in pregnancy

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Women are more prone to develop tuberculosis during pregnancy and in the post-partum period due to the biological changes that influence the tuberculosis epidemiology. Government Hospital for Women and Children, Institute for Obstetrics and Gynecology (IOG), Chennai, India. To find out the impact of tuberculosis in pregnancy. The data from case sheets of pregnant women admitted for obstetric care from January 1, 2015 through December 31, 2015 in, Government Hospital for women and children, Institute for Obstetrics and Gynecology (IOG) were scrutinised. The data from case records of pregnant women with past history and/or present history of tuberculosis and admitted for obstetric care were selected and these constituted the study group. The data of Pregnant women who had delivered or had been admitted on the same dates, formed the comparison group. The incidence of TB in pregnancy in this hospital, for the year 2015 was 0.36%. The symptom of breathlessness, was present in a significant number of women (p value 0.004). Complaints of fever and cough, commonly associated with tuberculosis was also present in a large number of women. The BMI range was lower in pregnant women with TB. Skeletal deformities and Pregnancy induced Hypertension were more often observed in women with TB in pregnancy, and TB in pregnancy was more often seen in primis (58%). The majority of women were aged below 25 years. Relapse of TB was seen in 18.2% of pregnant women. COPD/ Bronchial complaints, and the complication of Premature rupture of membranes was significant. The complication of placenta previa, and more important to note, among primigravid women was highly significant and present in 3.6% of women. Abortion rates were significantly high (p value 0.047). Term deliveries were less. More babies had low birth weight, and Lower APGAR scores which were below 6. Perinatal mortality was 9% . Still births were high [p value 0.057]. Hospital stay was longer in women with TB, for both periods from admission to discharge from hospital and from delivery of baby to discharge from hospital (p value 0.027 and 0.002). Health services should definitely include measures for TB prevention, diagnosis and treatment in all antenatal and postnatal clinics.

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Key words **: Tuberculosis, Pregnancy, morbidity.**

In 2015, the World Health Organization (WHO) estimated that there were around 10.4 million new Tuberculosis (TB) cases worldwide, of which 3.5 million were women[1].

In women, the risk of TB increases during pregnancy[2,3,4] and is also associated with higher rates of maternal and perinatal morbidity and mortality[2-7]. For a pregnant woman, infected with Human immunodeficiency virus (HIV), and with active TB, the risk of maternal mortality increases by nearly 300%, when compared to that of an HIV negative pregnant woman[8]. Maternal TB is associated with poor outcome of the baby such as small for gestational age and low birth weight[8,9].

Without treatment both pulmonary and extrapulmonary tuberculosis, lead to poor obstetric and perinatal outcomes[9,10].

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Tuberculosis in Pregnancy :

Women are more prone to develop tuberculosis during pregnancy and in the post partum period,due to the biological changes that influence the tuberculosis epidemiology.

In preparation to receive and nurture the foetal allograft. Pregnancy suppresses the T-helper 1 proinflammatory response. This may mask symptoms while, increasing susceptibility to new infection and reactivation of tuberculosis. After delivery, T- helper suppression reverses, and symptoms of tuberculosis are exacerbated. A large study recently found that early postpartum women are twice as likely to develop tuberculosis as nonpregnant women[11-13].

In pregnant women, tuberculosis is often undiagnosed until late in the disease process[7]. Women usually appear healthy and do not present with typical symptoms of tuberculosis. Clinical diagnosis of tuberculosis is difficult especially among pregnant women, as the symptoms are initially ascribed to pregnancy. Constitutional symptoms like lethargy, night sweats, loss of appetite, tiredness, fatigue are non - specific symptoms, related to the physiological response to pregnancy. HIV co-infection also contributes to masking of symptoms and atypical presenta-

tions[8]. Further extra pulmonary tuberculosis appears to be on the rise recently. Cases of TB involvement of breast, spine, peritoneum, kidneys, pelvis and meninges were reported in women during pregnancy and puerperium[12-17].

TB in pregnancy can be missed easily and remain undiagnosed and unreported due to lack of clinical awareness and diagnostic tests. The effect of TB on pregnancy may be influenced by many factors namely, the severity of the disease, the gestational age of pregnancy, at the time of diagnosis, the presence of extra pulmonary spread, HIV coinfection and delay in instituting anti-tubercular treatment.

The WHO estimated that every year, one million TB cases are missed in India[1].

Yet , if anti-tubercular treatment (ATT) is started early in pregnancy, the outcome is the same as that in non-pregnant patients !![1,1a,1b].

In 2011, the highest number of cases in pregnant women (44500 cases) was in India , and contributed to 20.6% of the global TB burden. The rate of TB disease in India was estimated to be 2.3 (1.6-3.1) per 1000 pregnant women[1,1a,1b]. Though there being a high burden of TB cases in India[1], there is a limited data available about the impact of TB in Pregnancy.

Thus, we sought to analyse the factors that affect the pregnancy outcomes among Pregnant women with TB using the available hospital records in the, Government Hospital for Women and Children, Institute for Obstetrics and Gynaecology (IOG), Chennai, India.

TB is known to reactivate during pregnancy and in early puerperium.v. So it was decided that to obtain relevant information of the effect of tuberculosis in pregnancy[5,17,18], the data from case records of pregnant women, admitted for obstetric care with past history of tuberculosis or history of tuberculosis diagnosed in the current pregnancy should be analysed .

The term tuberculosis in pregnancy refers to pregnant women with past history of tuberculosis or with history of tuberculosis diagnosed in the current pregnancy.

Background and Settings :

The metropolis, Chennai is the capital city of India's southern most state Tamil Nadu, with a population of approximately 7.08 million people.

Government Hospital for women and children, Institute of Obstetrics and Gynaecology is a large institution in Chennai, South India , with 1075 beds for in-patients . The institution is also the obstetrics and gynaecology department of Madras Medical College (MMC) and Rajiv Gandhi General Hospital (RGGH). An average of 1100 to 1300 deliveries are conducted every month and annually more than 15000 pregnant women are admitted here for confinement. It is a tertiary referral centre and pregnant women with severe high risk complications,from nearby urban and rural areas and neighbouring states, are referred here for treatment and also for management of labour. To provide appropriate care, for the pregnant woman, at labour, the hospital is equipped with a Labour Ward, Intensive Care Unit, Isolation Ward, and a High Dependency Unit, and a New born care ward with neonatal intensive care unit. Specialists, both physicians and surgeons from Madras Medical College RGGH, call over to the hospital , for examining the pregnant women with medical or surgical complications, and give expert advise regarding the management of these pregnant women. Chest and TB physicians from RGGH, provide the expert management for diagnosis and treatment of pregnant women with tuberculosis .

Aim :

To find out the impact of tuberculosis in pregnancy.

Methods :

Study population : For this study case records of women admitted for obstetric care in Government Hospital for women and children, Egmore Chennai, a tertiary referral, public, teaching hospital in the year 2015 from January 1, 2015 through December 31, 2015, were selected [study population].

Approval for this study was obtained from the, institutional, Ethics committee. Clearance was granted for us to access the obstetric records from the medical records department, for the year 2015.

Study design : This was a retrospective analytical case control study (Observational), and was conducted in 2016 from the months from August to December. Selection of case records for comparison was in the ratio of 4:1. Four records of women without history of tuberculosis were selected for every one record of woman with tuberculosis in pregnancy. This was to reduce statistical errors and for obtaining relevant values for the tests of significance.

Statistical Analysis was done by using SPSS software.

Selection of case records: The data from case sheets of pregnant women admitted for obstetric care in, Government Hospital for women and children, Institute for Obstetrics and Gynaecology (IOG) were scrutinised. The data from case records of all pregnant women with past history or present history of tuberculosis and admitted for obstetric care were selected and constituted the study group

For comparison the case records of women who had delivered on the same dates, or who had been admitted on the same date were selected. Selection was done by computer generated randomised numbers. This formed the comparison group. The details regarding pregnancy status, parity, gestational age of pregnancy, past history of abortion were noted. For pregnant women with history of treatment for tuberculosis in the past, the details regarding

completion of ATT course and when the anti tubercular treatment (ATT) was taken, were noted (ie, the number of years prior to the current pregnancy). The age, BMI, and socio economic status of women were recorded.

The presenting complaints common to TB, namely Breathlessness, Cough, Fever, Night Sweats, Weight loss and blood in sputum were noted for all women.

Sample size : In the study period of one year, a total of Fifty five pregnant women who had tuberculosis in the past or diagnosed with tuberculosis, had been admitted for obstetric care. They constituted the study group. In the comparison group there were 224 women admitted for obstetric care in the same period. This was to find out the significance of presenting complaints, and for delivered women , the outcome of pregnancy and neonatal outcome of babies born to pregnant women with tuberculosis.

Results :

In the study period of one year 2015 there were 15093 deliveries conducted, at Government. Hospital for women and children, Institute Of Obstetrics and Gynecology.

In the year 2015, the hospital recorded a maternal mortality rate (MMR) of 142 (maternal deaths per lakh deliveries). The perinatal mortality rate (PMR) per thousand was 63.1.

In the study period of one year, from January 1, 2015 through December 31, 2015, a total of Fifty five pregnant women who had or diagnosed with tuberculosis, were admitted for obstetric care. Twelve women were on treatment for TB and taking anti tubercular treatment, in the current pregnancy. Forty four women gave history of tuberculosis in the past. In the comparative group there were 224 women, without tuberculosis,admitted for obstetric care in the same period (Table 1).

The age group of women ranged from 19 to 35 years in the group of women with TB and from 18 years to 38 years[12,18], in the comparison group. Significantly high numbers of women with TB in pregnancy were aged above twenty four years and below 34 years (p value 0.001)[17,20]. The BMI range was lower among pregnant women with TB in the study group and ranged from 16 to 39 as compared to women in the comparison group without TB, where BMI ranged between 18 to 44. The largest number of twenty women among the study group with TB had BMI rates ranging between 18.5 to 24.9. As the hospital is a public, hospital and no money is charged from patients the majority of women in both groups were below poverty line. Both groups were comparable in socio economic status.

Symptoms :

It was important to note that the most common complaint of Breathlessness was complained of by a significant number of women[12,14,16,22] in the study group [p value 0.004]. Among other symptoms, Cough was complained of by a large number of women with TB (p value 0.069). Fever was present in more women with TB (p value 0.044). Other Complaints of weight loss, blood in sputum, night sweat was not complained of by any woman in either group. Primiparous women formed a significant group of 59% of women with TB in pregnancy (Table 1).

Maternal Complications :

Extrapulmonary TB affected 45.5% of women (n= 25), and among women with TB in the current pregnancy extrapulmonary TB was present in 58.3% of women. TB of lymph nodes of neck was the commonest type among this group.

Pulmonary TB affected 54.5% of women (n= 30) and was diagnosed in 41.7% of women with TB in current pregnancy.

Skeletal deformity in women was only present in four women with past history of being treated for TB[13,17]. Hypertension induced by pregnancy was an associated complication in a significantly large number of women with tuberculosis (p value 0.08). Relapse of TB in pregnant women was significantly high and seen in 18.2% of pregnant women. It was significant to note that tuberculosis relapsed during pregnancy even though these women had completed the course of anti tubercular treatment[18].

Pregnancy complicated by placenta previa was significant and observed in 3.6% of women. It was more important to note that, both these women were primigravidas. COPD/ Bronchial complaints, and Premature rupture of membranes was a significant complaint in women with TB[21-23].

Delivery :

The mode of delivery, as vaginal, assisted or by caesarean section was comparable in both groups (Table 2). Abortion rates were significantly high in the study group of women (p value 0.047).

Hospital stay was longer in women with TB, for both periods from admission to discharge from hospital and from delivery of baby to discharge from hospital (p value 0.027 and 0.002).

Baby Outcome :

The study group of women, recorded 80% live births and the comparison group had 98% of babies , born alive . Among the babies born to women in the study group only 67% were delivered at term, and only 62.5% of babies weighed 2.5Kg or more. The comparative group had 83% of babies born at term and 72% of them had birthweight of 2.5kg or more[13,19]. At birth APGAR scores of seven and above was recorded in only72% of babies in the study group and in 95% of babies in the comparison

Table 1— *Baseline Character of Pregnant women with TB and Pregnant women without TB admitted in Institute of Obstetrics and Gynecology, Egmore, Chennai for delivery in year 2015*

Factor		Pregnancy without TB		Pregnancy with TB		0R (95%CI)		0.001
		n	%	n	%			
Age	15-24	120	88.9	15	11.1	1.00		
	25-34	101	71.6	40	28.4	3.17	(1.65 - 6.07)	0.001
	35-44	3	75.0	01	25.0	2.67	(0.26 - 27.3)	0.409
BMI	< 18.5	3	37.5	5	62.5	1.00		
	18.5 - 24.9	82	80.4	20	19.6	0.15	0.03-0.66	0.013
	25.0 - 29.9	68	81.9%	15	18.1%	0.13	0.03 - 0.62	0.010
	30.0 & above	42	80.8%	10	19.2%	0.14	0.03 - 0.7	0.010
Socio Economic Status								
below poverty line		221	98.7	54	96.4	1.00		
above poverty line		3	1.3	2	3.6	2.83	0.46 - 17.4	0.262
							0.56 - 4.79	0.372
Presenting Complaints								
Breathlessness		2	0.9	5	8.9	11.33	2.13 - 60.09	0.004
Cough		5	2.2	4	7.1	3.5	0.91 - 13.52	0.069
Fever		9	4	3	5.4	1.41	0.37 - 5.38	0.619
Night Sweat		0	0	0	0		NA	
Weight Loss		0	0	0	0		NA	
Blood in sputum		0	0	0	0		NA	
Maternal Complications								
Anemia		42	18.8	11	19.6	1.06	0.51 - 2.22	0.879
Hypothyroidism		12	5.4	6	10.7	2.12	0.76 - 5.92	0.152
Pregnancy induced HT		20	8.9	1	1.8	0.19	0.02 - 1.41	0.104
Pre-eclampsia		16	7.1	5	8.9	1.27	0.45 - 3.64	0.651
Gestational diabetes		12	5.4	2	3.6	0.65	0.14 - 3.01	0.586
Precious Baby		6	2.7	3	5.4	2.06	0.5 - 8.49	0.319
Previous LSCS		41	18.3	10	17.9	0.97	0.45 - 2.08	0.938
Oligo hydromnias		29	12.9	8	14.3	1.12	0.48 - 2.61	0.791
Poly hydromnias		2	0.9	2	3.6	4.11	0.57 - 29.85	0.162
TB relapse		0	0.0	9	16.1			
Placenta Previa		0	0.0	2	3.6			
COPD|BA| bronchiectasis		4	1.8	5	8.9	5.39	1.4 - 20.79	0.014
Skeletal deformity		0	0.0	4	7.1			
Premature rupture of membrane		43	19.2	5	8.9	0.41	0.16 - 1.1	0.076
Heart disease complications		5	2.2	1	1.8	0.8	0.09 - 6.96	0.837
Cervical incompetence		0	0.0	1	1.8			
Thalassemia		2	0.9	1	1.8	2.02	0.18 - 22.66	0.569
Disseminated intravascular coagulation		26	11.6	5	8.9	0.75	0.27 - 2.04	0.569
HBsAg		10	4.5	1	1.8	0.39	0.05 - 3.08	0.368
HIV		2	0.9	0	0.0			

Among pregnant women with Tuberculosis, the symptom of breathlessness was significant. The BMI range was lower. COPD/ Bronchial complaints, and complication of Premature rupture of membranes was significant.The complication of placenta previa , and more important to note ,among primigravid women was highly significant and present in 3.6% of women.

group. Significant number of babies with Lower APGAR scores (below 6) were born to women in the study group (p value 0.37) . There were 5% of babies born dead in the study group and in the comparison group, it was 1%. The outcome of babies was similar to observations and studies done in other centres in the world[19-21]. Significantly more infant deaths was recorded in the study group (p value 0.057) (Table 3). Other features of baby complications such as birth asphyxia, IUGR, Respiratory Distress Syndrome, congenital anomalies and hypoglycemia were comparable in both groups[24-26]. At discharge only 77% of babies were alive in the study group ,although 95% of babies in the comparative group were discharged alive .

All HIV positive pregnant women are periodically screened for TB, according to the NACO guidelines, in this Institution. A total number of Forty seven, HIV positive women, delivered in this hospital during the study period. It was significant to note that no HIV positive mother was diagnosed with TB[28], both during pregnancy and in the post natal period, in the study period .

Maternal deaths due to TB.

In the study period there were no maternal deaths , wherein TB was the causative factor as either a direct or an indirect cause for maternal death.

Conclusion :

The incidence of TB in pregnancy was 0.36% ,in this study. On analysis of the symptoms and on following the course of pregnancy among women with tuberculosis (both in current pregnancy and history of disease in the past) we found the following. The symptom of breathlessness, was present in a significant number of women. Complaints of fever and cough, commonly associated with tuberculosis was also present in a large number of women. The BMI range was lower in pregnant women with TB. Skeletal deformities and Pregnancy induced Hypertension were more often observed in women with TB in pregnancy and TB in pregnancy was more often seen in primis. The majority of women were aged below 25 years. Relapse of TB in pregnant women was significantly high and seen in 18.2% of pregnant women. COPD/ Bronchial complaints, and Premature rupture of membranes was significant in women with TB.

The complication of placenta previa, and more important to note, among primigravid women was highly significant and present in 3.6% of women with TB in pregnancy. Abortion rates were significantly higher (p value 0.04).

Table 2 — *Pregnancy status, delivery outcome and hospital stay among women with TB in Pregnancy and pregnant women without TB , admitted in Institute of Obstetrics and Gynecology, Egmore, Chennai in year 2015*

Factor	Pregnancy without TB (n=224)		Pregnancy with TB (n=56)		0R (95%CI)		P value
	n	%	n	%			
Pregnancy Status							
P0	119	53.10	33	58.9		1.00	
P1	87	38.80	19	33.9	0.79	(0.42 - 1.48)	0.456
P2	16	7.10	3	5.4	0.68	(0.19 - 2.46)	0.553
P3	1	0.40	1	1.8	3.61	(0.22 – 59.21)	0.369
P4	1	0.40	0	0		NA	
Type of delivery							
Vaginal	125	55.8	21	37.5	1.00		
Forceps	13	5.8	2	3.6	0.92	(0.19 - 4.35)	0.912
LSCS	84	37.5	22	39.3	1.56	(0.81 - 3.01)	0.187
Abortion	1	0.4	2	3.6	11.9	(1.03 - 137.21)	0.047
No delivery	0	0	7	12.5		NA	
Not available	1	0.4	2	3.6		NA	
No of abortion							
0	197	87.9	46	82.1	1		
1	20	8.9	9	16.1	1.93	(0.82 - 4.51)	0.13
2	7	3.1	1	1.8	0.61	(0.07 - 5.1)	0.65
Type of delivery							
Vaginal	125	55.8	21	37.5	1		
Forceps	13	5.8	2	3.6	0.92	(0.19 - 4.35)	0.912
LSCS	84	37.5	22	39.3	1.56	(0.81 - 3.01)	0.187
Abortion	1	0.4	2	3.6	11.9	(1.03 - 137.21)	0.047
No delivery	0	0	7	12.5			
Not available	1	0.4	2	3.6			
Time Taken for (in Days) * Duration in Hospital Stay							
Admission to Delivery	1	0-2	1	0-1	1.03	(0.91 - 1.17)	0.597
Delivery to Discharge	6	4 - 8	9	6 - 12	1.1	(1.04 - 1.17)	0.002
Admission to Discharge	7	5 - 10	9	6 - 13.5	1.06	(1.01 - 1.11)	0.027

Definition of abbreviations: CI = confidence interval; OR = Odds ratio
Values were presented as n (%) and Median (Interquartile)
*Mann-Whitney test was performed Boldface indicates statistically significant at a = 0.05.

The outcome of pregnancy among pregnant women with TB: Abortion rates were significant, Term deliveries were less. Further , Hospital stay was longer in women with TB, for both periods from admission to discharge from hospital and from delivery of baby to discharge from hospital

Among pregnant women with TB ,term deliveries were less .The mode of delivery was comparable. Hospital stay was significantly longer in women with TB, for both periods from admission to discharge from hospital and from delivery of baby to discharge from hospital and (p value 0.027 and 0.002).

Perinatal mortality was 9% . The number of Still births was high (p 0.057). More babies had low birth weight . Lower APGAR scores below 6 were significantly high[19].

A pregnant woman living in poverty, overcrowding, malnutrition, food insecurity, tobacco use, HIV, or diabetes has a higher risk for adverse outcome of pregnancy. Women with TB face social stigma and discrimination by their families and communities. TB among women affect their children and families also. Cultural and financial barriers affect health seeking behaviour of women and lead to delayed diagnosis and to further severity of the disease[3].

Poor nutritional status, anaemia, hypo-proteinemia and associated medical disorders contribute to maternal morbidity and mortality[9]. TB in pregnancy continues as a cause of concern for both mother and baby. A simple clinical algorithm has been provided by WHO for identifying women at risk or with disease and so that they could be screened for tuberculosis, and providing for early diagnosis and treatment.

It is also important to address the unmet and basic needs of children , pregnant and breastfeeding women which should be done by national policy makers and health services implementing bodies.

Health services should definitely include measures for TB prevention , diagnosis and treatment in the antenatal and postnatal clinics[29].

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Table 3 — *Status of new-borns of TB Pregnancy Versus Pregnant women without TB admitted in Institute of Obstetrics and Gynecology, Egmore, Chennai in year 2015*

Factor	Pregnancy without TB (n=224)		Pregnancy with TB (n=56)		0R (95%CI)		P value
	n	%	n	%			
Baby Status							
Term	185	82.6	38	67.9	1.00		
Preterm	38	17	10	17.9	1.28	(0.59 - 2.79)	0.533
No delivery	0	0	2	3.6	NA		
Not available	1	0.4	6	10.7	NA		
Baby Weight							
<2.5kg	61	27.2	11	19.6	0.83	(0.4 - 1.74)	0.62
≥2.5kg	161	71.9	35	62.5	1.00		
Not available	2	0.9	10	17.9	NA		
Sex of the baby*							
Male	121	54	27	48.2	0.748		
Female	101	45.1	19	33.9			
Not available	2	0.9	10	17.9	NA		
APGAR Score							
Up to 6	5	2.2	4	7.1	4.24	(1.09 - 16.48)	0.037
7 to 10	212	94.6	40	71.4	1.00		
Not available	7	3.1	12	21.4	NA		
Status of birth							
Alive	220	98.2	45	80.4	1.00		
Death	3	1.3	3	5.4	4.89	(0.96 - 25.01)	0.057
Not available	1	0.4	8	14.3	NA		
Status of discharge							
Alive	213	95.1	43	76.8	1.00		
Death	10	4.5	5	8.9	2.48	(0.81 - 7.61)	0.113
Not available	1	0.4	8	14.3	NA		
Birth complications							
Birth asphyxia*	3	1.3	0	0			1.000
IUGR	14	6.3	3	5.4	1.08	(0.3 - 3.92)	0.911
Respiratory distress	17	7.6	3	5.4	0.9	(0.25 - 3.2)	0.865
Congenital anomalies	16	7.1	1	1.8	0.3	(0.04 - 2.35)	0.254
Hypoglycaemia	2	0.9	1	1.8	2.6	(0.23 - 29.28)	0.44
Number of days in NICU*							
	2	1- 5	3	1 - 8			0.232

Definition of abbreviations: CI = confidence interval; OR = Odds ratio;
NICU = Neonatal Intensive Care Unit
Values were presented as n (%) and Median (Interquartile)
*Fishers Exact test and Mann-Whitney test was performed
Boldface indicates statistically significant at a = 0.05.

Outcome of infants born to women with tuberculosis: The number of Still births was high. More babies had low birth weight . The numbers of infants with Lower APGAR scores below 6 were significantly high. At discharge only 77% of babies were alive in the study group ,and 95% of babies in the comparative group. Perinatal mortality was high [9%].

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