

A survey of pregnant women with tuberculosis at the Port Moresby General Hospital

SHIRLEY HEYWOOD¹, APEAWUSU B. AMOA², GLEN L. MOLA¹ AND CECIL A. KLUFIO^{1,3}

SUMMARY

From March 1995 to February 1998, 110 patients diagnosed with tuberculosis (TB) in pregnancy or the puerperium at the Port Moresby General Hospital (PMGH) were surveyed. 96% were diagnosed as a result of the symptoms of tuberculosis, 4% through contact tracing. 11 of 40 patients who first attended antenatal clinic in the second trimester were not diagnosed until after delivery. The mean birthweight of term infants of TB patients was significantly less than term infants in a previous survey at PMGH. 45% of babies were growth restricted. With increasing duration of treatment, both increasing maternal weight gain in pregnancy and higher mean birthweight were found. Maternal and perinatal mortality were high in the study patients. There were 6 maternal deaths and a perinatal mortality rate of 137/1000. The majority of maternal and fetal losses occurred in patients who had pulmonary, miliary and meningeal TB. Improvement in the detection of tuberculosis in antenatal patients and the introduction of adequate treatment before delivery should prevent maternal deaths and perinatal morbidity and mortality.

Introduction

The interaction between tuberculosis (TB) and pregnancy has been debated for centuries. Some have proposed a deleterious effect on the pregnancy outcome and disease progression while others have considered tuberculosis to have a benign or beneficial effect on the course of pregnancy (1).

With the advent of effective medical treatment for tuberculosis this debate has become less important. Most experts now believe that with adequate treatment of the pregnant woman with tuberculosis the prognosis of the pregnancy should not be affected adversely by the presence of the disease (2). However, pronounced adverse perinatal outcome is associated with late diagnosis, incomplete treatment and advanced pulmonary lesions (3).

In most of the developed world the incidence of tuberculosis was falling until the

mid-1980s when, with the co-epidemic of HIV infection and the increase in immigration of people from countries where TB is still endemic, the number of new cases began to rise. This has led some authorities to consider screening of antenatal patients at high risk of tuberculosis infection (4).

Tuberculosis is a disease of considerable public health importance in Papua New Guinea (PNG). At the Port Moresby General Hospital (PMGH) it is the most common cause of death in the medical wards (5). In 1995 the TB Clinic registered nearly 2000 new patients of whom one-quarter were women of child-bearing age. The Obstetrics and Gynaecology Division of PMGH annual reports show that tuberculosis contributes 1-2 maternal deaths each year, and that 10-15 cases of TB in pregnancy are diagnosed in the antenatal clinics supervised by the hospital amongst 9000 booked mothers each year. However, it is suspected that many cases of TB in pregnancy still remain undiagnosed.

¹ Division of Obstetrics and Gynaecology, Department of Clinical Sciences, Faculty of Medicine, University of Papua New Guinea, PO Box 5623, Boroko, NCD 111, Papua New Guinea

² Division of Obstetrics and Gynaecology, Port Moresby General Hospital, Free Mail Bag, Boroko, NCD 111, Papua New Guinea

³ Present address: University of Ghana Medical School, PO Box 4326, Accra, Ghana

The objectives of this study were to determine the prevalence of tuberculosis in pregnancy and the puerperium at the PMGH; to determine how the diagnosis of tuberculosis was made; to assess the perinatal and maternal outcomes; and to document the management modalities used for the mother and her infant.

Method

This was a descriptive longitudinal survey. The study population included all women attending Port Moresby General Hospital Antenatal Clinic and other urban clinics in the city and all patients delivered at Port Moresby General Hospital, or admitted in the puerperium. All patients diagnosed to have tuberculosis during pregnancy or puerperium were enrolled. A total of 110 women were recruited between March 1995 and February 1998. Patients were interviewed using a pre-tested questionnaire. Further information was obtained from the patients' antenatal record card, TB records, labour ward record book and inpatient records.

The variables studied included sociodemographic characteristics such as age, ethnic region, area of residence, education and occupation, medical and obstetric history, family history of tuberculosis, presenting clinical condition and investigations performed, gestational age at diagnosis, treatment given to the mother and its duration, maternal weight gain, the outcome of the pregnancy, breastfeeding and management in the puerperium.

Results

Between March 1995 and February 1998, 110 women were enrolled into the study. 70 (64%) were antenatal, 23 (21%) postnatal and

17 (15%) had been previously discharged from the hospital or delivered elsewhere.

The age of the women ranged between 15 and 41 years with a mean of 25.8 years. 75% were under 30 years of age.

Table 1 shows some of the socio-demographic characteristics and parity of the study patients in comparison with the 1993 survey of all parturients in the PMGH labour ward (6). There were more parous women in the TB group than in the total parturients (80% vs 64%) and more of the TB group were from the Southern Region (86% vs 70%) and were village dwellers (34% vs 10%).

TABLE 1

PARITY, ORIGIN AND EDUCATIONAL STATUS OF 110 TUBERCULOSIS PATIENTS IN COMPARISON WITH TOTAL PARTURIENTS AT PORT MORESBY GENERAL HOSPITAL IN 1993

	TB patients N (%)	1993 parturients (%)
Para 0	22 (20)	36
Parity >4	14 (13)	7
Southern Region	95 (86)	70
Highlands Region	11 (10)	18
Village dwellers	37 (34)	10
Education nil	31 (28)	24
Education grade 1-6	48 (44)	43
Higher education	8 (7)	3

Table 2 shows the past history of TB diagnosis and the duration of treatment received. 28 patients (25%) had a past history of TB. Of the 28 patients, 16 (57%) had been

TABLE 2

PAST HISTORY OF TUBERCULOSIS AND TREATMENT RECEIVED IN 28 PATIENTS

Years since diagnosis	Complete treatment	Incomplete treatment	Total
1-2 years	6	10	16
3-10 years	6	2	8
More than 10 years	4	0	4
Total	16	12	28

TABLE 3

INTERVAL BETWEEN DIAGNOSIS OF CONTACT AND THE INDEX PREGNANCY OF PATIENTS WITH TUBERCULOSIS AND THE RELATIONSHIP BETWEEN PATIENTS AND THEIR CONTACTS IN 57 TB PATIENTS WITH A POSITIVE CONTACT HISTORY

	1-2 years	3-10 years	>10 years	Total
Parent	9	7	9	25
Sibling	4	3	1	8
Other relative	5	3	3	11
Patient's child	4	2	0	6
Husband	0	2	0	2
Other person	4	1	0	5
Total	26	18	13	57

diagnosed within the 2 years prior to the index pregnancy. Only 6 of these 16 had completed their treatment.

57 women (52%) had a positive contact history of TB. Table 3 shows the years between the contact and the index pregnancy and the relationship between the study case and the TB contact. 25 (44%) of these contacts were parents. 26 (46%) of the contacts were diagnosed less than 2 years previously.

The vast majority of the patients (96%) were investigated and diagnosed as a result of symptoms or signs suggestive of tuberculosis. Only 4% were diagnosed because of contact tracing.

The most common symptoms experienced were chronic cough (85%), weight loss (76%), intermittent fever (69%), night sweats (64%), lethargy (65%) and enlarged or discharging lymph nodes (18%). Other symptoms included chronic headache with vomiting (in TB meningitis) and aphonia in 2 patients with TB laryngitis. 6 women had ascites, 77% had evidence of weight loss and 79% had chest signs.

Of the four patients diagnosed by contact tracing, one had no symptoms or signs but was found to have a positive sputum and one first presented when she brought her sick baby to the hospital at 3 months of age. The baby had TB and the mother had weight loss, respiratory symptoms and a sputum positive for acid-fast bacilli (AFB). The third patient had a

suspicious chest X-ray and a positive Mantoux test on screening but negative sputum for AFB and the fourth had enlarged lymph nodes that were positive for TB on biopsy.

92 patients (84%) had chest X-rays suggestive of TB including 8 with miliary TB.

81 women had sputum cultured and of these, 48 (59%) were positive.

Table 4 shows the gestational age when the diagnosis of TB was made and the trimester during which the patient first attended the antenatal clinic. 13 of the 14 patients diagnosed during the first trimester had been diagnosed in the medical wards or clinics and then referred for antenatal care.

There was in many cases a delay between the first antenatal attendance and the diagnosis of tuberculosis. 40 patients first attended the antenatal clinic during the second trimester. Of these, 18 were not diagnosed until the third trimester and 11 were only diagnosed after delivery. This led to delay in commencing treatment and in 2 cases the patients discharged themselves from the postnatal ward without treatment and follow-up arrangements.

85 women had at least one recorded weight measurement. The mean weight at first visit was 53.9 kg with a range of 32 kg to 83 kg. 75 women had subsequent recorded weights. Table 5 shows the weight gain in pregnancy in relation to the duration of TB treatment. 19 patients (25%) had no treatment. Of these, 6

TABLE 4

DIAGNOSIS BY GESTATIONAL AGE AND WHETHER DIAGNOSIS WAS MADE BEFORE, DURING OR AFTER ANTENATAL CARE

Gestational age at diagnosis	Diagnosed before ANC	1st trimester booking	2nd trimester booking	3rd trimester booking	Total
0-12 weeks	13*	1	-	-	14
13-27 weeks	7	2	11	-	20
28-42 weeks	3	1	18	19	41
Labour or PN	-	0	11	7	18
Total	23	4	40	26	93

* Includes 1 patient diagnosed before pregnancy who completed treatment during pregnancy

ANC = Antenatal Clinic

PN = postnatal

(33%) lost weight and only 2 (10%), both of whom had TB in cervical lymph nodes only, gained 0.5 kg/week or more. Another 19 patients had treatment for 4 weeks or less; 7 (37%) lost weight and 3 (16%) had an adequate weight gain. 37 (49%) had treatment lasting more than 4 weeks; of these, only 4 lost weight whilst 23 (62%) gained 0.5 kg/week or more.

65 women (60%) had other antenatal complications, the most common being anaemia, intrauterine growth restriction, preterm labour, malaria and fetal death in utero. Only 1 patient was HIV positive, though HIV screening was not performed on all patients in the study. There was 1 patient with placenta praevia and 1 with twin pregnancy.

The gestational age at delivery was recorded

in 108 cases. This ranged from 18 to 42 weeks with a mean of 37 weeks. In many cases, when the woman first attended clinic late and menstrual dates were unknown, gestation at delivery was estimated by Dubowitz assessment of the neonate performed by the paediatricians. 7 patients (6%) delivered between 18 and 28 weeks gestation. A further 36 patients delivered before term, 4 (4%) between 29 and 33 weeks and 32 (30%) between 34 and 37 weeks. 65 infants (60%) were delivered at term (38 to 42 weeks).

There were few complications in labour. 5 patients had thick meconium staining of the liquor. In 2 of these the fetal heart recording was abnormal. 1 baby died during labour: the mother first presented in labour and was subsequently diagnosed to have Addison's

TABLE 5

WEIGHT GAIN IN PREGNANCY ACCORDING TO THE DURATION OF TREATMENT

Duration of treatment	Weight loss	<0.5 kg/week	≥0.5 kg/week*	Total
No treatment	6 (33%)	11 (57%)	2 (10%)**	19
4 weeks or less	7 (37%)	9 (47%)	3 (16%)	19
>4 weeks	4 (10%) [†]	10 (28%)	23 (62%)	37
Total	17 (23%)	30 (40%)	28 (37%)	75

* A weight gain of 0.5 kg/week in the 3rd trimester is considered an adequate weight gain

** Both patients had positive lymph nodes only

[†] 2 patients took treatment in the first half of pregnancy but defaulted from treatment; 1 patient who was noncompliant with treatment throughout died postnatally; and 1 with cor pulmonale died postnatally

disease causing her profound hypotension. There were 2 patients with transverse lie and 1 who had epileptic fits associated with meningitis.

Recorded birthweights ranged between 250 g and 3750 g (mean 2420 g \pm SD 668 g). 46 of the babies (45%) were growth restricted. The mean birthweight of infants of more than 37 weeks gestation was 2621 g \pm SD 623 g (95% confidence interval 2482-2760). In comparison with the mean birthweight of normal term babies delivered at the PMGH between 1987 and 1989 (7), the mean birthweight of babies of TB patients was significantly smaller ($z=8.6, p<0.0000$).

25 babies were admitted to the special care nursery. 2 had major congenital anomalies and died in the first week. 3 had respiratory distress possibly due to meconium aspiration syndrome. The remainder were of low birthweight (<2000 g). Duration of admission was between 1 and 64 days with a mean duration of 18 days. There were 6 early neonatal deaths including 2 from major

congenital anomalies.

26 mothers had postnatal complications. 3 presented to the hospital with puerperal sepsis, 2 with allergic reaction to treatment, 1 with Addison's disease, 3 with puerperal pyrexia and the remainder with other septic complications or anaemia. There were 6 maternal deaths.

The major forms of TB in this study were 82 pulmonary, 8 miliary, 6 lymph nodal, 6 pleural, 4 abdominal, 2 meningeal, 1 spinal and 1 pericardial. Several had more than one site involved.

Patients with pulmonary, miliary or meningeal TB had the worst outcome, both maternal and fetal.

All deliveries before 28 weeks were in cases with pulmonary or meningeal TB. Among the 109 patients with known pregnancy outcomes, there were 7 mid-trimester losses, 5 fetal deaths in the third trimester or in labour and 10 postnatal deaths. There were 5 maternal deaths and 1 late maternal death that occurred 5

TABLE 6

MATERNAL AND PERINATAL MORTALITY AMONG THE TB PATIENTS AND THEIR BABIES

	A (n=16)	B (n=20)	C (n=29)	D (n=45)
Mean bwt a	1946 g	2278 g	2400 g	2728 g
Mean bwt b	1865 g	2207 g	2243 g	2608 g
12-28 week loss	3	1	1	2
MSB	1	0	1	1
FSB	1	0	1	0
Neonatal death	0	3	2	4*
Maternal death	1 (6%)	1 (5%)	2 (7%)	2 (4%)**
PNM/1000	154 [†]	150	143	109*

A = No antenatal care, no TB treatment before delivery

B = Antenatal care, no TB treatment before delivery

C = Antenatal care, 4 weeks or less TB treatment before delivery

D = Antenatal care, more than 4 weeks treatment before delivery

Mean bwt a = mean bwt of all infants of 28 or more weeks gestation

Mean bwt b = mean bwt of infants of mothers with miliary, pulmonary or meningeal TB of 28 or more weeks gestation

* 2 deaths due to lethal congenital anomaly

** Both patients had cor pulmonale

[†]1 infant death also at 2 months of age

bwt = birthweight

MSB = macerated stillbirth

FSB = fresh stillbirth

PNM = perinatal mortality

months after delivery from TB meningitis in a patient who defaulted from treatment.

Table 6 compares the pregnancy outcomes both maternal and fetal according to whether or not the mother received antenatal care and treatment of tuberculosis during pregnancy. Group A (16 patients) had no antenatal care and TB diagnosis was made after delivery. Group B (20 patients) attended antenatal clinic but received no TB treatment before delivery. Group C (29 patients) received antenatal care and TB treatment for 4 weeks or less. Group D (45 patients) received TB treatment for more than 4 weeks. The mean birthweight for all babies over 28 weeks gestation is shown. The birthweight of all patients (bwt a) shows a trend of increasing weight as length of treatment increases, from 1946 g in group A to 2728 g in Group D. Mean bwt b is the mean birthweight of infants of mothers with miliary, meningeal or pulmonary tuberculosis (ie infants of patients with pleural, spinal, lymph node and abdominal TB excluded). It can be seen that the birthweights of babies of these mothers is lower in all groups, but shows a similar trend of increasing weight with increasing duration of treatment. The perinatal mortality rate was 154/1000 in Group A, 150/1000 in Group B, 143/1000 in Group C and 109/1000 in Group D (2 out of the 5 perinatal losses in Group D were due to lethal congenital anomalies: 1 baby had Edward's syndrome and 1 had congenital heart disease). The overall perinatal mortality rate was 137/1000.

2 mothers died from TB meningitis. 1 patient with pulmonary TB was noncompliant with treatment throughout the pregnancy and refused further treatment after delivery; she died at home 3 weeks later. 1 mother, who had no antenatal care, had a massive haemoptysis and cardiac arrest shortly after delivery. Both maternal deaths in group D were patients who had received long-term TB treatment but had severe cor pulmonale which deteriorated postnatally.

Treatment regimens

At the start of this study the standard treatment regimen lasted 6 months: 2 months daily quadruple therapy (A regimen) with rifampicin (10 mg/kg), ethambutol (15 mg/kg),

pyrazinamide (1500-2000 mg) and isoniazid (5 mg/kg), followed by 4 months twice weekly rifampicin and isoniazid with pyridoxine (B regimen). This regimen was altered, due to a change in the treatment protocol of the TB Clinic during the course of the study, omitting ethambutol from the A regimen and continuing the B regimen for 7 months. In individual cases where the response to treatment was slow, the A regimen was continued for 3 months or the B regimen was given daily.

All mothers were encouraged to breastfeed. 87 babies were breastfed. Failure to breastfeed was due to maternal illness or death or the infant's poor health. 85 babies received prophylactic treatment. 54 were given prophylactic isoniazid for 3-6 months. The results of the paediatric follow-up are not known. It is the official policy that all babies receive BCG vaccination at birth, whether isoniazid is given or not. After the 6 months of isoniazid treatment a Mantoux test is performed and BCG vaccination given to babies who test negative. This is because poor compliance with follow-up means that many of these babies will not be seen at the six-month appointment. There were no neonatal complications noted due to maternal or infant treatment.

Discussion

This survey has confirmed our observation that tuberculosis is more common among our pregnant women than earlier statistics suggested. The results indicate that, when TB is adequately treated, a good outcome, both maternal and fetal, can be expected. In untreated, belatedly treated or inadequately treated disease, however, there is high fetal and maternal morbidity and mortality.

As other studies have found, poor compliance is a major problem in TB control, resulting in inadequate treatment and the danger of development of drug resistance (8). A number of patients in this study had been diagnosed previously but did not complete treatment. Two maternal deaths could have been avoided if the patients had complied with treatment.

Tuberculosis patients should be advised to avoid pregnancy until their treatment is

complete. TB Clinic staff should ascertain family planning use of all women patients between 15 and 45 years from the beginning of TB treatment. When a patient is not using any family planning method she should be offered appropriate advice. Depo-provera may be the most acceptable method for these patients who already need to take a large number of tablets each day. Rifampicin may reduce the effectiveness of the combined oral contraceptive pill (COP) due to hepatic enzyme induction. Women who have been using the COP should either change to a higher dose pill, such as Microgynon 50, or consider another method such as Depo-provera. Patients with significant lung damage should be advised against further pregnancy and a sterilization procedure offered.

Those who become pregnant need to be aware that they should continue and complete their treatment. Attendance at antenatal clinic should be encouraged from early pregnancy. Two women in the study had discontinued treatment when they realized they were pregnant and, as this did not come to the attention of the medical team for many weeks, they had to commence a further full course of treatment.

The two main treatment regimens used in the study showed no difference in pregnancy outcome. The standard treatment protocol was changed in accordance with World Health Organization (WHO) guidelines (9). The three drugs, rifampicin, isoniazid and pyrazinamide, are considered adequate unless there is drug resistance.

Isoniazid and rifampicin are safe in pregnancy in humans. Ethambutol has not been found to be associated with an increase in fetal anomaly (10). Pyrazinamide has now been in widespread use for a number of years without any demonstrable hazards. Streptomycin is associated with greater than 10% incidence in eighth cranial nerve damage in the fetus and is contraindicated throughout pregnancy (11).

The detection of all cases of TB proved to be a problem. Most of these cases were detected due to symptoms and this almost certainly means that there were a number of

cases that were not detected. This increases the risk of deterioration in the mother's condition postnatally and communication of the infection to the infant. Even among patients with significant symptoms or signs, this survey found that there was often a delay between the patient's first antenatal presentation and the investigation and diagnosis of the disease.

There is a need in Port Moresby to consider a screening policy other than the present one of history and examination alone. Midwives, nurses and paramedical workers usually provide antenatal care in PNG. An easily administered and non-time-consuming means of alerting the health worker to the possibility of TB is required if we are to detect and treat the disease earlier and reduce the preventable maternal and fetal mortality and morbidity we see at present. In a study in USA of culture-proven tuberculosis patients, those who were pregnant were more likely to be detected by routine skin testing, to be symptom free and to be smear negative, than the non-pregnant patients (4). The US authors recommend routine skin testing for antenatal patients in high-risk groups. In USA, BCG is not given to the whole population for TB prophylaxis. In PNG most antenatal mothers will have received BCG vaccination in infancy. This would complicate the interpretation of Mantoux test results

A brief screening questionnaire is being considered whereby a TB risk score will be allotted. This would include symptoms such as coughing for more than 3 weeks, haemoptysis, weight loss and the presence of lymphadenopathy or chest signs, and positive TB contact within the last 2 years. Patients with a high risk score would be investigated with sputum examination and chest X-ray.

There is also a need to improve family screening and education of patients and their families. Most patients in this study who had a family history of tuberculosis had not been screened for the infection.

Better education and family support will hopefully improve compliance with treatment. The introduction of directly observed therapy (DOT) has been found in some studies to improve compliance (12). In the DOT scheme

a member of the community is chosen to supervise the patient's medication. In Port Moresby this scheme is currently being introduced. In some areas community supervision has been started while in others the supervisor is a family member. We await the response to this changed approach to the treatment of tuberculosis.

REFERENCES

- 1 **Miller KS, Miller JM Jr.** Tuberculosis in pregnancy: interactions, diagnosis, and management. *Clin Obstet Gynecol* 1996;39:120-142.
- 2 **Starke JR.** Tuberculosis. An old disease but a new threat to the mother, fetus, and neonate. *Clin Perinatol* 1997;24:107-127.
- 3 **Jana N, Vasishta K, Jindal SK, Khunnu B, Ghosh K.** Perinatal outcome in pregnancies complicated by pulmonary tuberculosis. *Int J Gynaecol Obstet* 1994;44:119-124.
- 4 **Carter EJ, Mates S.** Tuberculosis during pregnancy. The Rhode Island experience, 1987 to 1991. *Chest* 1994;106:1466-1470.
- 5 **Naraq S, Gena M.** Mortality at the medical wards of a university teaching hospital in Papua New Guinea: a study of 1242 admissions. *PNG Med J* 1989;32:171-176.
- 6 **Kluffio CA, Amoa AB, Kariwiga G.** A survey of Papua New Guinean parturients at the Port Moresby General Hospital: sociodemographic and reproductive characteristics. *J Biosoc Sci* 1994;26:185-190.
- 7 **Kluffio CA, Kariwiga G, MacDonald R.** Normal birthweight at Port Moresby General Hospital: a retrospective survey of normal term births to determine birthweight distribution. *PNG Med J* 1992;35:10-16.
- 8 **Pozsik CJ.** Compliance with tuberculosis therapy. *Med Clin North Am* 1993;77:1289-1301.
- 9 **World Health Organization.** Treatment of Tuberculosis. Guidelines for National Programmes. Geneva: World Health Organization, 1993.
- 10 **Brost BC, Newman RB.** The maternal and fetal effects of tuberculosis therapy. *Obstet Gynecol Clin North Am* 1997;24:659-673.
- 11 **Nelson-Piercy C, Waldron M, Moore-Gillon J.** Respiratory disease in pregnancy. *Br J Hosp Med* 1994;51:398-401.
- 12 **Anderson GD.** Tuberculosis in pregnancy. *Semin Perinatol* 1997;21:328-335.