

A SURVEY OF THE RELATIONSHIP OF INFECTION WITH TOXOPLASMOSIS IN ASIAN WOMEN AND ITS POSSIBLE EFFECTS ON THEIR PREGNANCY OUTCOME

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SYNOPSIS

A group of pregnant Chinese, Indian and Malay women, whose pregnancies had terminated unsuccessfully, were studied to relate infection with toxoplasmosis to their adverse pregnancy outcomes.

The incidence of infection was high, especially in the young Malays. Possible reasons for this could be due to acquiring the disease through contaminated meat and close contact with domestic animals, there being a large reservoir of animal infestation. Local climatic conditions are favourable for the survival of the infective oocyst.

The incidence of abortion was higher in patients with raised toxoplasma antibodies. A relationship with low birth-weight infants and congenital abnormalities was probably not significant, but infection may be a factor in unexplained neonatal death and still-birth.

In order to clarify the role of toxoplasmosis possible lines of investigation, management and advice are suggested, concerning the patient with a poor pregnancy outcome. Enlisting co-operation of both paediatrician and parasitologist may improve foetal morbidity and mortality associated with this parasitic infection.

INTRODUCTION

Perinatal morbidity and mortality has been markedly reduced in the last decade as a result of intensive antenatal and intrapartum care, aided by sophisticated monitoring apparatus and biochemical tests of placental function. Nevertheless, there is still fetal wastage occurring either in utero, during the neonatal period, or from congenital anomalies all of obscure aetiology.

Certain uncommon parasitic diseases, well recognised by parasitologists, and neglected by obstetricians and paediatricians, have been known for many years to have a deleterious effect on the fetus. In order to further improve fetal survival, attention should now be directed towards these more exotic conditions in an attempt to solve the problem of unsuccessful pregnancies, due to obscure causes. Toxoplasmosis is one of these parasitic infections which may seriously effect the fetus in utero or later in

infancy and adolescence. Due to its relative rarity and because of paucity of knowledge of its life-cycle and transmission to man, study of this ubiquitous parasite in relation to pregnancy has been neglected. Maternal infection may be associated with recurrent abortions, unexplained intrauterine deaths and congenital abnormality; also it is well recognised for its serious cerebral and ophthalmic manifestations in the infant and adolescent.

MATERIALS AND METHODS

Whilst in the Royal Army Medical Corps the author was stationed in Singapore between October 1969 and February 1970, and during this time 84 pregnant Asian patients were surveyed to investigate a possible relationship between toxoplasmosis and a poor pregnancy outcome. Criteria for inclusion in the survey was a previous history of or the pregnancy under review terminating in more than one abortion; an abortion occurring between the 16th to 28th week of pregnancy; delivery of an infant weighing 2500 grams or less; a still birth or neonatal death or an infant with congenital abnormality.

Selected patients were personally interviewed and where possible informed of the reason for

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the questionnaire, which recorded details of the patient's place of birth, ethnic origin and the countries that she had resided in. Details of previous illnesses including unexplained fevers, tropical diseases and contact with pets were recorded. In addition an accurate account, as far as was possible, of the previous and the present pregnancies. The patient was examined for the presence of lymphadenopathy, hepatosplenomegaly and the fundi for the presence of chorioretinitis. With the consent of the patient 10 mls of venous blood was collected in a plain bottle for examination by the indirect haemagglutination reaction (H.I. test) of Jacobs and Lunde (1958). By dividing the patients into two groups, those with a positive test and those with a negative test hereafter referred to as positive and negative reactors, the negative reactors were used as controls. At delivery cord blood was collected from the positive reactors and subjected to the indirect haemagglutination test. In addition maternal and cord blood was collected from any patient who had not been surveyed antenatally, but at delivery produced an infant whose condition satisfied the criteria for inclusion in the survey. In a few cases of abortion the brain of the fetus was examined for the presence of the toxoplasms, but in these particular cases their presence was not demon-

strated. The patients surveyed included 40 Chinese 19 Indian, 21 Malay and 4 Nepalese, who were either attending the British Military Hospital or the Kandang Kerbau Hospital of Singapore.

RESULTS

Of the 84 patients, 33 (39.3%) were found to be positive reactors and 51 (60.7%) were negative reactors. Fig. 1 is a histogram comparing the positive and negative reactors grouped by race and age. In the Chinese and Indians the majority of positive tests occurred in the age group of 20 to 35 years, but in Malays the greater proportion of positive tests were in a much younger age group.

Fig. 2 compares the haemagglutination titre levels in the various racial groups, showing that the young Malays had the higher titres.

Table I gives details of the past and present pregnancy outcomes of the positive reactors. The patients have been placed in age groups and the totals of the various pregnancy outcomes for the past pregnancies and the pregnancy under review are given. The percentages in the previous pregnancy outcome refer to a percentage of the total number of each patient's pregnancies i.e. the combined number of abortions, low birth weight infants and normal

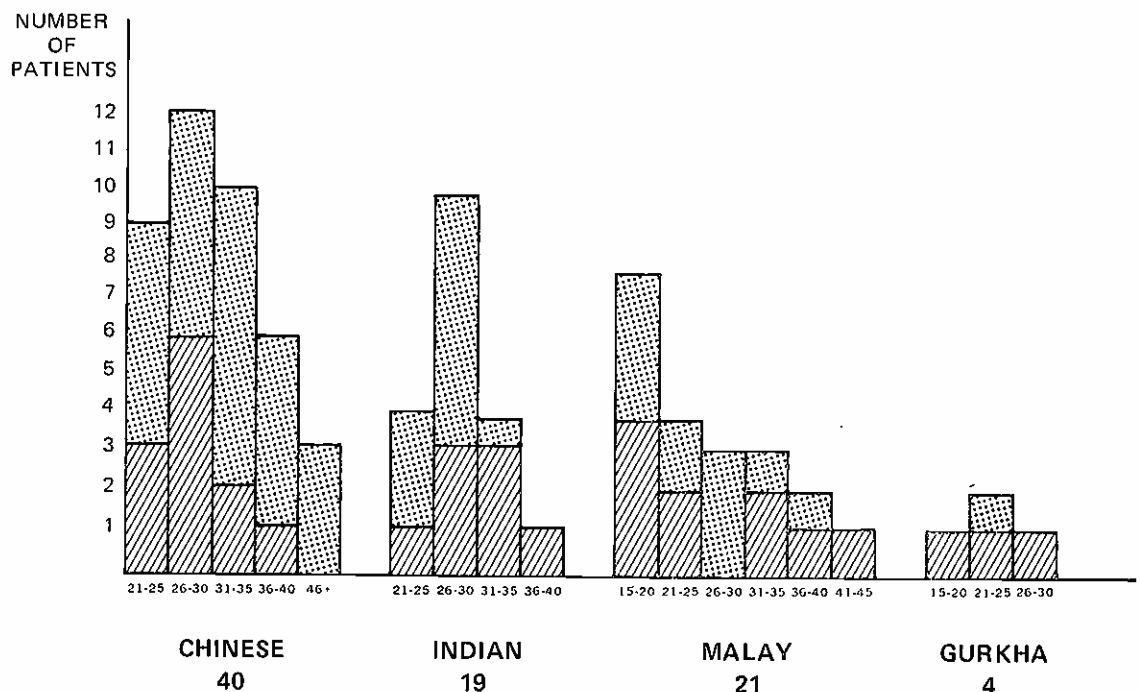


Fig. 1. A comparison between the four Asian races of positive and negative reactors grouped by age. Positive reactors are coloured red; negative green.

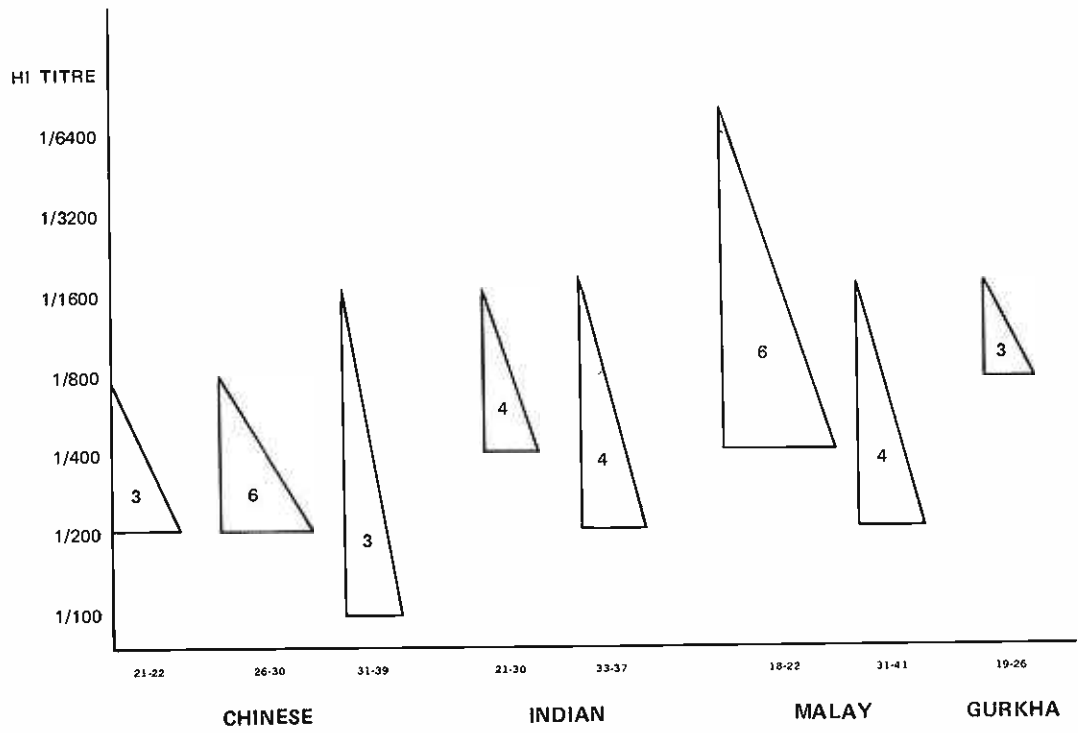


Fig. 2. Comparing the different titre levels of the four Asian races. The patients have been grouped by ages and each triangle represents the various levels of titres found in a particular age group. The figure in the triangle is of the number of patients in the group.

TABLE III
84 ASIAN POSITIVE AND NEGATIVE REACTORS

Comparison of the pregnancy outcomes showing the outcomes for which no cause could be demonstrated

	POSITIVE REACTORS				NEGATIVE REACTORS			
	P.O.H.		P.P.		P.O.H.		P.P.	
Number of Patients Surveyed	33		27		51		38	
Number of Pregnancies	115		27		139		38	
Pregnancy Outcome		%		%		%		%
Abortion	28	24.5	2	7.4	26	18.5	1	2.6
<2500G	14	12.2	10	37.0	28	20.0	15	39
>2500G	69	60	13	48	82	59	13	34
C.A.	2	1.7	—	—	1	0.7	—	—
S.B.	9	7	2	7.4	3	2	3	7.9
N.N.D.	7	6.1	—	—	4	2.9	—	—
A.	70	60	22	81	99	71	29	76

P.O.H. = Previous obstetric history.

P.P. = Present pregnancy under review.

TABLE I
ASIAN POSITIVE REACTORS

Showing previous pregnancy outcomes and known present pregnancy outcomes of surveyed patients grouped by age

Age Group	No. of Patients	No. of Preg's. ctes.	PREVIOUS PREGNANCY						PRESENT PREGNANCY								
			Ab.	<2500	>2500	C.A.	S.B.	N.N.D.	A.	No. of Patients	Ab.	<2500	>2500	C.A.	S.B.	N.N.D.	A.
15-25	12	17	6	4	7	1	1	10	11	2	7	2					
26-30	10	34	6	5	23		5	17	8		3	5					
31-41	11	64	16	9	39	1	3	43	8		2	6					
Total	33	115	28	18*	69	2	9	70	27	2	12*	13					
Percent.			24.5	15.7	60	1.7	7.0	60		7.4	44.5	48					

* Four L.B. weight infants cause known.

† N.N.D. due to anencephaly.

Abbreviations: Ab. = Abortion, C.A. = congenital abnormality, S.B. = Stillbirth, N.N.D. = Neo-natal death, A = alive.

* Two L.B. weight infants cause known.

† N.N.D. due to R.D.S.

TABLE II
ASIAN NEGATIVE REACTORS

Showing previous pregnancy outcomes and known present pregnancy outcomes of surveyed patients grouped by age

Age Group	No. of Patients	No. of Preg's. ctes.	PREVIOUS PREGNANCY						PRESENT PREGNANCY								
			Ab.	<2500	>2500	C.A.	S.B.	N.N.D.	A.	No. of Patients	Ab.	<2500	>2500	C.A.	S.B.	N.N.D.	A.
15-25	16	16	5	3	8		2	9	14	3	10	1					
26-35	26	72	18	18	36	1	4	45	19		10	9					
36-48	9	51	3	10	38		2	45	5		2	3					
Total	51	139	26	31*	82	1	6†	99	38*	3†	22‡	13					
Percent.			18.7	22.2	59	0.7	4.3	71		7.9	58.0	34					

* Cause for 3 L.B. Wt. infants known.

† Cause for 3 S.B. infants known.

‡ Four N.N.D. causes known.

* 13 patients lost to follow up.

† Cause for 2 abortions known.

‡ Cause for 7 L.B. Wt. infants known.

†† One S.B. Accidental Haemorrhage.

** Two N.N.D. Respiratory Distress Syndrome.

weight infants. In the present pregnancy the percentage is that of the number of patients whose pregnancy outcome was known.

In the previous obstetric history 24.5% of the pregnancies terminated in abortion. Eighteen (15.7%) of the infants were of low birth weight, one being an anencephalic, two were twins and the fourth was 'small for dates' being associated with a maternal chronic urinary tract infection. Details of the remaining 14 were unobtainable. The two congenital anomalies were hydrocephalus and anencephaly. Of the nine stillbirths no details could be obtained. There were eight neonatal deaths, one due to anencephaly, and of the remaining seven details could not be obtained.

Of the pregnancy under review details of the outcome were obtained from 27 patients only, as six were lost to follow up. Two patients aborted (7.4%) both were Malays, one with four previous abortions and a H.I. titre of 1/3200 and the other a primigravida with a titre of 1/1600. Amongst the 12 (44.5%) infants of low birth weight the cause was undetermined in 10, but due to placental insufficiency in two. The two still births were of unknown cause, one in a Gurkha with a H.I. titre of 1/1600 and the other an Indian with a titre of 1/200. The neonatal death occurred in a Gurkha induced for placental insufficiency at term and the 'small for dates' infant died from respiratory distress syndrome.

Table II shows the details of the past and present pregnancies of the negative reactors. Eighteen per cent of their previous pregnancies terminated in abortion; there were 31 (22.2%) infants of low birth weight, two were twins, one was the result of induction for severe pre-eclamptic toxæmia (PET) at 36 weeks and details of the remainder were unobtainable. The congenitally abnormal infant had a meningomyelocele. Of the still births, one was due to intra-cranial haemorrhage consequential to a ventouse delivery, two followed concealed accidental haemorrhage and in the remaining three the cause was undetermined. Four of the eight neonatal deaths were undetermined, three of the remainder were due to respiratory distress syndrome and one to a meningomyelocele.

In the negative reactors' pregnancy under review 13 of the 51 patients were lost to follow up. Of the remaining 38 patients, three (7.9%) aborted, one spontaneous, one due to cervical incompetence and the third at 26 weeks due to

retro-placental haemorrhage. Of the 22 (58%) low birth weight infants the cause was determined in seven. Two were due to placental insufficiency, one had congenital syphilis, one was premature the mother having severe infectious hepatitis, another resulted from concealed accidental haemorrhage at 36 weeks and the remaining two followed surgical induction in mistaken maturity. Of three of the four still births three were undetermined, but one was due to accidental haemorrhage. Both neonatal deaths were due to respiratory distress associated with prematurity.

In Table III the positive and negative reactors have again been compared, but known causes for unsuccessful outcomes have been excluded and the percentages altered accordingly. This has been done in order to observe whether there was a significant difference in the poor pregnancy outcomes of the positive reactors compared to the negatives, who had shown no serological evidence of having been exposed to toxoplasmosis. There was a significantly higher incidence of previous abortion in the positive reactors, being 24.5% compared to the negatives of 18.7%, and in the pregnancy under review 7.4% of positives aborted compared to 2.6% of the negatives. It is of interest that of the positive reactors, two Malays with H.I. titres of 1/3200 one had had a previous abortion and the other, having had four previous abortions, aborted in the present pregnancy, One Chinese with a titre of 1/1600 had aborted twice previously and an Indian with a titre of 1/1600 had had five previous abortions. Further two Malays with titres of 1/1600, one had had two previous abortions and the other aborted in the pregnancy under review.

No significance could be attached to the incidence of low birth weight infants, as details of previous pregnancies were unavailable in both groups. In the pregnancies under review the incidence was similar in both groups.

There was a slightly higher incidence of congenital abnormalities in past history of positive reactors, 1.7% as compared to 0.7% of negatives. There were no congenital abnormalities in the present pregnancies.

Again due to insufficient details about previous pregnancies little significance could be attached to the higher incidence of still births of the positive reactors compared to the negatives—7% to 2%. In the pregnancy under review, the incidence was similar.

Although neonatal death occurred more frequently in previous history of the positive reactors, 6.1% compared to 2.9% of the negatives, no conclusions could be drawn as details were incomplete.

CONCLUSIONS

Certain contributory factors could account for the high rate of infection amongst Asians, especially Malays. There is a known reservoir of toxoplasma amongst their domestic animals, in particular the pig (Tan and Zaman 1973), and human infection is recognised to be acquired through undercooked, contaminated meat (Desmonts *et al*, 1965, Jacobs *et al*, 1960, and Catar *et al*, 1969). The author recently conducted a survey of British Service dependents stationed in Germany, where toxoplasmosis is prevalent and where pork and raw steak are popular dishes. These wives showed a high presence of antibody compared to those who had not been resident in Germany. The warm moist climate of the tropics favours survival of the oocyst form of the parasite (Baruzzi 1970, and Fleck 1963).

Although abortion is a frequent occurrence in tropical countries, the higher incidence amongst positive reactors confirms the findings of Jones *et al* (1966) and Kimball *et al* (1971). In fact the author also found a similar relationship to recurrent abortion amongst the German women and wives stationed in Germany in his survey, thus confirming the findings of Johnston (1965). Some workers, notably Langer (1963), Remington (1964) and Werner (1966), have demonstrated the toxoplasma in aborted material from mothers with positive tests.

Owing to a multiplicity of causes the Asian infant is of lighter birth-weight than that of the Western mother's baby. Without more detailed study it would not be possible, at present, to incriminate toxoplasmosis.

Although it was found that mothers with positive tests had previously delivered more congenitally abnormal infants than the negative reactors, the rate was no higher than to be expected. These were mainly neural tube malformations commonly found in women of low socio-economic status, nevertheless it may be of interest that cases of anencephaly have been associated with toxoplasmosis (Hoffbauer and Schmidtke 1963).

In spite of the increased incidence of unexplained stillbirths and neonatal deaths in the

previous pregnancies of the positive reactors, possibly related to other factors, no conclusions could be reached incriminating the parasite.

Although the number of patients surveyed was small and therefore no statistical evaluation was possible, it would seem significant that toxoplasmosis could be responsible for some abortions and may play a role in the aetiology of unexplained stillbirth and neonatal death. With liaison between obstetrician, paediatrician and parasitologist when investigating patients with poor pregnancy outcomes, some of the questions concerning the mode of transmission of this infection, its life-cycle and the role of the acute and chronic infection in pregnancy may be answered. Antenatal patients could be screened for the presence of antibody to toxoplasmosis; at delivery the cord bloods of the infants of the positive reactors could be tested and if found to be positive the re-examination, of the infant's blood at six weeks is recommended to exclude antibody transference. Should the blood be positive again then the infant requires follow up by paediatrician and ophthalmologist to detect the early signs of toxoplasmosis. Patients who have had a poor pregnancy outcome and are found to have a raised antibody titre could very well be treated in the non-pregnant state with pyrimethamine, sulfadimidine and steroids. Finally, it would be prudent to advise our pregnant patients to avoid the handling and the eating of undercooked meat, and in addition they should avoid intimate contact with domestic animals, especially the cat.

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