CLINICAL PRESENTATION OF TOXOPLASMOSIS IN PREGNANT WOMEN

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SUMMARY

426 consecutive pregnant women were studied to note the prevalence of toxoplasmosis in a private practice. An evaluation of the role of toxoplasmosis in pregnancy was done. 388 cases had the test for toxoplasmosis performed. The methods employed to detect IgG and /or IgM antibodies were Indirect Haemagglutination, or Indirect Immunofluorescent Antibody methods, or ELISA technique.

21.7% had significant antibody titres at the primary test. 11.1% of 388 cases were at risk of prenatal/perinatal transmission of toxoplasmosis. Almost all these cases were treated with pharmacological agents. The pregnancy/foetal outcome by risk groups were analysed for past and current pregnancy outcome. Those with high and rising titres of antibodies had greater unfavourable outcome. Pregnancy outcome among the treated and the untreated risk groups was further compared; and timely treatment of this infection seemed to improve the pregnancy outcome.

From this analyses, it can be established that toxoplasmosis is quite prevalent and that it plays an important role in determining pregnancy/foetal outcome. Routine test for toxoplasmosis in pregnancy is warranted.

Introduction

The significant role, infections belonging to the TORCH group, plays in causation of prenatal/perinatal insults is well established. Toxoplasmosis is one such common infection (Whitfield, 1986). Majority of women have silent subclinical infection (Couvreur and Desmonts, 1983). The most serious consequences of the infection are seen in the offspring of women who acquire infection during pregnancy (McCabe and Remington, 1983). Active infection in the early pregnancy often results in foetal death, abortion, congenital malformation and intra-uterine growth retardation; while foetal transmission of the infection during the last trimester is

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more likely to produce child with subclinical congenital toxoplasmosis (Lee R.V., 1988). The child may show signs of mental retardation and physical handicap in later life.

Background

Interest was aroused in Bombay since 1984 when the detection of toxoplasmosis was done by serology using Indirect Haemagglutination Antibody or Indirect Immunofluorescent Antibody methods. Amongst the several serious effects of prenatal transmission of infection to the foetus, repeated foetal loss was thought to be one. Therefore, women with previous foetal wastage were initially considered for investigations. During the years 1984 and 1985, very few cases were investigated. From 1986, serious attempts to pick up cases, both at Nowrosjee Wadia Maternity Hospital (NWMH) and Hospital For Wommen Care (HFWC) in Bombay, were made. At NWMH, 882 tests revealed among the patients with previous pregnancy wastage, that the Indirect Haemagglutination Antibody (IHA) method showed a positive test at 1:64 titre in 31.4%, and at 1:256 titre in 16.8%. All patients at the higher titre were considered as at high risk. Corresponding figures at HFWC for 1986 were 16.9% and 5.6%. All women with bad obstetric history and titre for toxoplasmosis at 1:256 were then treated. Pregnancy loss was significantly reduced subsequent to treatment at both hospitals. Since,, 1987 April, the ELISA technique and test for detection of IgM became available and these modified the approach to the problem of toxoplasmosis in pregnancy.

Aims and Objectives

The purpose of this study was to note the prevalence of toxoplasmosis in the Indian population and to evaluate the effects of the disease in pregnant women. The effect of the timely treatment on the perinatal outcome was further studied.

Materials and Methods

Out of 426 consecutive pregnant women in a private practice, 388 (91.1%) had the test for toxoplasmosis done. The accepted significant titre for IgG antibody was 1:64, and that of IgM was 1:10 or its equivalent.

The cases were divided according to the tests done for antibody detection in three groups (Table I), Group A- IgG and IgM performed; Group B- IgM only; and Group C- IgG only. The following three methods were employed to detect the antibodies: (i) ELISA for IgG and IgM - 175 cases, (ii) Indirect Immunofluorescent Antibody (IFA) for IgG and IgM - 82

TABLE - I
SHOWING 3 GROUPS OF CASES ACCORDING TO THE PRIMARY TESTS PERFORMED AND THE SIGNIFICANT ANTIBODY TITRES

Group	*Test Performed*	*No.*	*Significant Titres*	
			No.	*Percent*
A	IgG & IgM	49	25 (IgG)	51.0
B	IgM only	23	8 (IgM)	34.8
C	IgG only	316	51 (IgG)	16.4
	Total	388	84 (21.7%)	

cases, and (iii) Indirect Haemagglutination Antibody (IFA) for IgG only - 131 cases. The tests were done at different times in pregnancy depending on time of patient reporting and her agreeing to get the test performed. Ninety eight (26%) reported in the first trimester, 100 (26%) in the second trimester, and 181 (48%) in the third trimester. In nine cases the time of the test was not specified. In all cases in which IgG titre was significant, either a repeat IgG or an IgM test was done. All cases with significant titres for IgM or rising titres for IgG, were decided to be treated. The treatment in all cases was commenced after 14 weeks of gestation, to avoid possible harmful effects of drugs in the first trimester. Three types of treatment schedules were employed: (i) Pyrimethamine 25 mg., twice a day, for 3 weeks - 21 cases, (ii) Pyrimethamine 25 mg. and Sulphadiazine 500 mg., twice a day, for 3 weeks - 28 cases, and (iii) Rovamycin (spiramycin) 4 Tablets a day, for 3 weeks - 2 cases.

Results and Observations

Of 388 cases, 84 (21.7%) had significant titres (Table I). Results of the primary tests were, as shown in Table I. In Group A, 25 of the 49 cases had significant IgG titres (51%). In these 25 women, IgM was positive in 8 cases (32%); four of the remaining 17 cases had raised IgG or positive IgM at a repeat test. In group B, eight of the 23 cases had significant IgM titres (34.8%); and, in Group C, of the 316 cases, 51 had significant titres of IgG (16.4%). Thirty three of these 51 cases had either a repeat IgG or an IgM test, and among these, 23 had either a raised IgG or a positive IgM titre (69.7%)

Therefore, considering all the 388 pregnant women in whom test for toxoplasmosis was performed, 43 cases (11.1%) were at high risk for prenatal/perinatal transmission of infection:- Group A, 12 cases; Group B, 8 cases; and, Group C, 23 cases. All these 43 women were requested to take treatment after completion of 14 weeks of pregnancy. Thirty nine received full course, while four women either did not accept it or gave it up due to side-effect. 12 more patients in whom only a single test of IgG showed titre of 1:64 or higher were also treated because of previous pregnancy wastage. In all 20 patients were prescribed in the 2nd trimester, and 35 in the 3rd trimester.

Previous Pregnancy Wastage in 388 Patients

Table II shows the previous pregnancy wastage in 388 patients under study

TABLE - II
SHOWING PREVIOUS PREGNANCY WASTAGE BY "RISK" GROUPS

Risk Group	*No.*	*No. of past pregnancies*	*Abortion*	*Fetal Loss*	*Preg. Loss%*
High Risk Titre IgG	43	34	4	5	26.5
1:64 & more Titre IgG	41	29	5	3	27.6
Less Than 1:64	30	26	9	2	42.3
Negative	274	189	41	10	27.0

by toxoplasmosis risk groups. The pregnancy/foetal loss was exceptionally high in the group of cases who had low titres for IgG. This may mean that, during earlier pregnancies, the infection was active and untreated resulting in pregnancy loss. In the groups with higher titres, the infection should be more recent, and its harmful effect is not reflected in the past pregnancies.

Current Pregnancy / Foetal Outcome in 426 Cases

Table III shows the present pregnancy outcome as related to the condition of foetus in four test results groups. Negative cases and those with insignificant titres in Table II have been grouped as negative in Table III. All cases with major congenital malformation in which abortion or foetal loss had occurred, have been listed as pregnancy wastage. It can be seen that there is a high percentage of total cases of unfavourable foetal outcome in the high risk group. It is not so in cases with only high IgG titres. Though the numbers are less, there is a trend indicating that each of the problems, namely, intrauterine growth retardation, preterm delivery, congenital malformation, and abortion/foetal loss, are greater in the high risk group of 43 cases compared to the other groups.

Pregnancy Outcome in Treated and Untreated Risk Groups

While 39 of the 43 women in the high risk group had received treatment, only 12 qualified for treatment in the high IgG titre group (Table - IV). The differences in

TABLE - III
SHOWING PRESENT PREGNANCY OUTCOME AS RELATED TO FOETUS IN THE FOUR TESTS RESULTS GROUPS

Test Group	*No.*	*Foetal Outcome*					*Total Problems Percentage*
		IUGR	*Preterm-AGA*	*Cong. Malf.*	*Abrt.*	*F. Loss*	
High Risk	43	4	3	1	2	1	25.6
IgG more than 1:64	41	1	1	–	–	1	9.8
IgG less than 1:64 & Negative	304	18	12	1	3	6	13.2
Not done	38	2	2	–	–	1	13.2

TABLE - IV
SHOWING FOETAL RESULTS BY TREATMENT IN THE RISK GROUPS

Risk group	*No.*	*Treatment +*			*No Treatment*		
		No.	*Poor fetal result**		*No.*	*Poor fetal Result*	
			No.	*%*		*No.*	*%*
High Risk	43	39	9	23.1	4	2	50.0
High titre	41	12	1	8.3	29	3	10.3
Low titre	30	–	–	–	30	5	16.7

the number of unfavourable pregnancy outcome were noted in the treated and the and the untreated cases. In the high risk group, timely treatment showed better results. In the group of cases with significant IgG titres, this could not be said; more stringent selection of cases for treatment in this group may be needed in future.

Other Maternal Infections in 426 Pregnant Women

The following other infections were noted in the women under study:

1. Pyrexia of unknown origin	10 cases	2.4%
2. "FLU"	6 cases	1.4%
3. Urinary tract infection	27 cases	6.3%
4. Upper respiratory infection	4 cases	0.9%
5. Malaria	9 cases	2.1%
6. Infectious hepatitis	3 cases	0.7%

To compare the prevalence of toxoplasmosis with other infections, the above rates are given. Not a single case of syphilis was recorded, though V.D.R.L. test was routinely done. Test for detection of cytomegalic virus infection had been sporadically done; out of seven tests performed, two were positive, two showed low antibody titres, and three were negative. Similar figures for chalmydia infection showed one out of seven was positive, one borderline, and five negative. Three cases tested for Rubella antibody showed two already immunised, and one was negative.

Discussion

The finding of 11.1% of pregnant women at risk for prenatal/perinatal transmission of toxoplasmosis is very significant. Routine test for the infection is warranted in all pregnant women.

The diagnostic test of IHA method being the least expensive and readily performed at ordinary laboratory, made it quite popular. This method, however, has several limitations, such as, it has been frequently negative in documented cases of toxoplasmosis especially early in the infection (Welch et al. 1981). This test is hence not the most desired for screening of pregnant women.

The high incidence of pregnancy loss in the past associated with low titre (less than IgG) indicates perhaps active infection in earlier pregnancy resulting in the mishaps.

The current pregnancy problem were more in the high risk group. In the group of significant IgG titres not but indicating high risk, the pregnancy problems were not greater than those in the remaining cases. Since the majority of cases in the high risk group were treated, it is difficult to say what would have happened if treatment was withheld. Though there is indication that treatment in the high risk group does benefit, further clarification is necessary in larger series. Ethical consideration may not permit withholding of treatment for clinical trial. Studies in France (Desmonts, G. and Couvreur J., 1974 and 1979) confirm that women infected before conception and treated had no evidence of abortion, still births, infection caused by toxoplasmosis. While treatment of acute or recent maternal toxoplasmosis appears to reduce the risk of foetal wastage and congenital infection (Lee, R., 1988), caution is advised with Pyrimethamine and Sulfonamides in the first trimester of pregnancy.

Ideally, during pregnancy, tests should be done early in the first trimester and if negative, tests should be repeated at about 28 weeks of pregnancy to note if

infection has occured subsequently in pregnancy. By this practice, all cases of active or recent infection can be diagnosed and treated in time. It is worthwhile recollecting that immunity following one infection of toxoplasmosis is short-lived. Reinfection, therefore, is possible in subsequent pregnancy. Tests are recommended in each pregnancy.

Besides toxoplasmosis, the study has indicated that several other infections occur during pregnancy and it may be that two infections may be concurrently present in the same pregnancy. Each of these infections play its own role in unfavourable outcome of pregnancy. Larger multicentric studies with easily available diagnostic laboratories are undoubtedly required in Indian population.

Conclusion

Prevalence of past or prevent toxoplasmosis infection in Indian populations may be quite significant. Vegetarian diet is no protection against the infection, as all food can be contaminated. The concern for active/recent toxoplasmosis in pregnancy, its prenatal/perinatal transmission, and, treatment of pregnant women should arouse obstetricians to pay more heed to its detection. Infants born of mothers with active toxoplasmosis and with significant IgG titres, need to be followed up to document the deleterious effects in them as years pass by.

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