REVIEW OF LITERATURE
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The term bad obstetric history is applied to a pregnant mother where her present obstetric outcome is likely to be affected adversely by the nature of previous obstetric disaster. The previous fruitless conception should be obstetrically related and as such mishaps to baby due to some other reason should not come to the preview of BOH. It includes previous history of premature delivery, still birth, abortion and congenital malformation.

BOH is a distressing problem affecting approximately 1% of all women. The most significant increase in risk occurs after the first miscarriage. The risk of miscarriage in nulliparous women and those who have had a successful pregnancy rises from approximately 5% to over 20% after one miscarriage. The risk increases there after with each successive miscarriage reaching over 40% after three consecutive losses. (Regan, L.; Breurde, P.R. 1989; Kunde, U.B., Hansen V., 1991).

Bad Obstetric History can be due to:

There are recognized courses of BOH that include hormonal disorder (thyroid disease and luteal phase defect). Chromosomal anomaly in one or both parents, uterine infection and possibly uterine anatomical defect (Stray Pedersen
and Stray Pedersen 1984; Daya et al 1988; Daly et al 1983; Toth et al 1986).

- Chromosomal abnormality of the embryo is the most common cause of sporadic miscarriage. A women with history of repeated pregnancy loss. Chromosomal abnormalities of embryo occur much less frequently (Bave J., Bave A., 1973).

- Heavy alcohol consumption (Sabal, R.J.; Miller, S.I., 1980; Kline, J.; Shraut, P., 1980).

- Heavy smoking (Parazzini F., 1987)

- Embryo supposed to implant in avascular part of endometrium in case of uterine septum leading to arrested development (Harger J.H., 1983).

- Destructive Mullerian fusion such as double, uterus, septate or Bicornuate uterus (Bennert M.J., 1967).

- Cervical incompetence (DeCherney, A. et al 1987)

- Diethylstilboestrol exposure in utero (Kaufman, R.H. Adam E., 1980).

- Menstrual disorders and infertily are the presenting hallmarks but recent evidence shows that Asherman's syndrome may cause recurrent pregnancy loss (Schenker, J.G et al 1982).

- Myomas are associated with an increased risk for obstetric complication including miscarriages, preterm
labour, ruptured membranes, abnormal fetal presentation (Babaknia A et al 1984).

- A rare endocrine etiology for early pregnancy losses in maternal hyperandrogenicity (Badarau, L. 1972).

- In insulin dependent diabetic women with inadequate glucose control have two to threefold higher rate of recurrent pregnancy loss as compared to general population of women (Whettaker, P.; Tayler, A., 1982).

- Thyroid dysfunction is often an aetiological factor for recurrent pregnancy loss (Winikaff, D., 1982).

- Luteal phase deficiency is an important cause of early pregnancy loss (Csapo, A.I. 1972, 78 & Rabinsersan, D. Taher, M., 1992).

- Mycoplasma Hominis and Ureaplasma urealyticum have been associated with recurrent pregnancy loss (Stey Pedersen, 1984).


- Listeria monocytogenes infection can cause spontaneous abortion, preterm labor and neonatal infection (Rappaport, F.; Rabinovits, M. 1960).
- Herpes simplex virus and cytomegalovirus are two virus which can cause habitual abortion (Kriel, R.L., 1970).

- Malaria during pregnancy is associated with spontaneous abortion, still birth, low birth weight and prematurity (Lewis, E. 1973).

- Primary infection with toxoplasma can cause foetal death and miscarriage (Faulen W., 1990).

- Incompatible ABO group mating may be responsible for early pregnancy wastage and often recurrent but Rh incompatibility is a rare cause of death of foetus before 28th week.

- Chronic hypertension leads to foetal malnutrition preterm labour and abruptio placental which can cause sudden intrauterine death of foetus (Lindheimer, M.D. 1985) and Arias F. 1975, 1979).

- Chronic renal disease can cause placental vascular insufficiency which can cause preterm birth and foetal growth retardation (Cunningham, F.C. 1990).

- Anaemia during pregnancy is associated with preterm births, still births and neonatal deaths (Raszkowski, I.; Wajacick, J., 1966).

- Presence of circulating antiphospholipid antibody is a marker for poor pregnancy outcome (Gatenley, P.A. et al 1989).
Mothers producing antipaternal blocking antibodies that have complement dependent or antibody dependent lymphocytotoxicity. These antibodies have a protective effect and absence of these cause pregnancy rejection (Oksenberg J.R. et al, 1993).

**Historical Aspect of Toxoplasma Gondii:**

Toxoplasma was discovered by Nicole and Monceaux in 1908 in a small rodent gondii (Clenodactylus gondii) of Africa. Human importance of organism was realised 30 years after i.e. from the year 1939. Although 2 cases were reported in the interval one in 1914. Castellavi from Sri Lanka and other in 1923 by Jonku. Toxoplasma gondii was first recognized as a cause of congenital infection and disease by Janku in Chachoslovakia in 1923.

We now realize that it is cosmopolitan in the human population and can cause disease. The importance of the organism as a human pathogen has stimulated a huge amount of research in recent years.

Thus the one time obscure protozoan parasite of an obscure African rodent has become one of the most exciting subjects in parasitology.

Toxoplasma gondii is an intracellular protozoan parasite. It was placed in subphylum sporozoa in 1964 by Society of Protozoologist.
Morphology, Biology and life cycle:

Toxoplasma gondii is a delicate ovoidal, pyriform or crescentic body measuring 4 to 6 microns long by 2 to 3 microns wide with one or both extremities pointed or rounded. With Giemsa's or Wright's stain it has a blue stained cytoplasm containing a rounded red stained mass of chromatin in the nucleus.

In human infections the organism is found in smear of exudates and in the granulomatous tissue either singly free or intracellular or in cyst like masses. T. gondii is a parasite of endothelial cell, leukocytes, body fluids and tissue cells of the host such as cardiac and skeletal muscle, alveoli, cells of the kidney tubules intestinal mucosa, liver parenchyma: endothelial and reticular cells and neurons.

(French, J.K., 1973) - Life cycle includes intestinal epithelial (enteroepithelial) and extraintestinal stage in domestic cats and other felines. But extra intestinal stage only in other hosts. Sexual reproduction of toxoplasma occurs while in cat and only asexual reproduction is known while in other hosts.

Extraintestinal stage begins when a cat or other host ingests bradyzoits, ingested tachyzoits or sporocysts also some times are infective. Entero epithelial stage are
initiated when a cat ingests zoitocysts containing bradyzoites, oocysts containing sporozoites or occasionally tachyzoites.

ENTERIC CYCLE:

Hutechison et al (1970) observed schizogenic and Gametogenic stages of T gondii inside epithelial cells of small intestine (ileum) of domestic cat. Large number of oocyte were found in the infected cat faeces.

Schizogony and gametagony occured in the epithelium of tip of intestinal villi. They usually develop in the ileum (the commonest site of infection) but the whole intestine can be affected about 4-29 merozoites are found inside the schizont. The merozoit liberated from the rupture of schizont may continue their cycle of schizogony while other develop into micro and macrogometacytes, after fusion and division these sexual form give rise to oocyte.

EXENTERIC CYCLE:

The oocyte containing 2 sporocyst are excreted in cat faeces for about 1-2 week. On maturation sporocyst develop into 4 sporozoites resembling trophozoites and become infective to man and other animals. The oocyte after ingestion liberate sporozoite which is heterologous hosts penetrate mucosal cells of the intestine and the prolifer-
tive stage of the parasite and is responsible for causing extensive damage to tissue in which it develops.

According to Hoase, C.A. (1972) two forms of toxoplasma are found in man.

1- **Tissue cyst or extracellular form** : It may be found free in the tissue fluids. Some of the sporozoits and also the endozoits tend to localise in the central nervous system and the musculature where they are transformed into tissue cysts inside which the parasites also multiplies.

2- **Pseudocyst or Intracellular form** : It is found in the cells of RE system and many nucleated cells.

**MODE OF INFECTION (Transmission)**;

According to Jacob (1968) human toxoplasmosis can occur in two way.

(A) **Congenital** : The most tragic form of this disease is congenital toxoplasmosis. Toxoplasma can cross placental barrier from the mother's blood and affect developing foetus.

(B) **Acquired** :

1) Ingestion of undercooked meat containing tissue cyst. In countries like France where raw meat is popular the infection rate is high (Hughes, H.P.A., 1985).

2) By inoculation (through skin) contact with infected tissues of animals, toxoplasma can penetrate through cracks
and small abrasion in the skin. Sheep and swine may be likely source of infection in man if handling or testing of meat prior to cooking is done - Work, 1971.

3) By accidental ingestion of oocytes that had been shed in a cat's faeces - Flies can contaminate food with viable oocytes for up to 48 hours after contact with cat faeces (Wallace, G.D. 1971).

Clinical feature:

The disease toxoplasmosis has been recognised both as a neonatal infection and as an acquired infection in children and adults. Antibody to toxoplasma is widely prevalent in human throughout the world yet clinical toxoplasmosis is less common. Most infection are asymptomatic and mild. Several factors influence this phenomena the virulence of strain of toxoplasma, the susceptibility of the individual host, age of host and degree of acquired immunity of the host.

Symptomatic infection can be classified as acute, subacute and chronic.

In most acute infections the intestine is the first site of infections, first extraintestinal sites to be infected are mesentric lymph node and the parenchyma of liver. Most common symptom of acute toxoplasmosis is painful swollen lymph glands in cervical, supraclavicular and
inguinal regions. This symptom may be associated with fever, headache, muscle pain, anaemia and sometimes lung complications. This syndrome can be mistaken easily for Blue. If immunity develops slowly the condition can be prolonged and is then called subacute, tachyzoites cause extensive lesion in lung, liver, heart, brain and eyes.

Chronic infection results when immunity builds up sufficiently to depress tachyzoite proliferation, cysts can remain intact for years and produce no obvious, clinical effect, host may develop symptom of chronic encephalitis, blind spots, cyst rupture in retina can lead to blindness. Other are myocarditis with permanent heart damage and pneumonia. In immunocompetent person it can cause disseminated disease.

**IMMUNOLOGY OF INFECTION**

Quantitative studies of immunoglobulin profile reveals that the initial response in acute acquired toxoplasmosis is the elaboration of Ig M antibodies with in first 20 days of infection, this type of antibody peaks and then diminishes quantitatively with the appearance of specific antibodies of the Ig G type. In chronic toxoplasmosis the antibody is exclusively Ig G (Jones M.H., Sever J.L., 1966).
The fetus in utero responds to infection with *T. gondii* by elaborating Ig M antibodies. This response may result in an overall elevation of Ig M level in the cord serum as well as the presence of specific Ig M antibodies.

**DIAGNOSIS:**

*T. gondii* is an obligate intracellular parasite. All methods to cultivate it on synthetic media have been unsuccessful. *T. gondii* has been successfully grown in tissue culture of rat embryo heart by Lack (1955) and by other workers in embryonic ovin tissue. Pulvertaft et al. 1954 grew the parasite on murine tissue (bone marrow, lymph node). Intraperitoneal inoculation of a biopsy of lymph node, liver of spleen into mice is useful and accurate.

For many years the routine serological method for toxoplasmosis had been the methylene blue dye test often referred as Babin-Feldman dye test. The disadvantage of this otherwise sensitive test is the necessity of using living organism potentially infectious to the laboratory worker (Sabin & Feldman, 1948).

In direct fluorescent antibody would be the test of choice in the clinical laboratory provided that the equipment for fluorescent microscopy is available. If the laboratory is not so equipped the alternative serological method would be indirect hemagglutination test (Peter G Beach et al. 1978).
The complement fraction test can contribute in making a serodiagnostic interpretation from a single serum sample but itself is not a good diagnostic method because of the long delay, upto two months in becoming positive after exposure (Alexand Macdonald 1950).

Demonstration of specific antibody using an enzyme linked immunosorbent assay is easy and accurate method (Van Loon, A.M. et al 1980).

**Toxoplasmosis in pregnancy:**

Congenital toxoplasmosis was first reported by Jacoby and Saçenin (1948) in Britain. Complement fixing and neutralising antibodies were present in some apparently healthy women (Macdonald 1949).

Cathie & Dudgeon (1949) recognise a number of sign which suggest congenital toxoplasmosis but themselves these signs are insufficient for diagnosis which call for laboratory investigation and to obtain some guidance on the incidence of infection.

Sabin and Feldman (1949) investigated the dye test and complement fixing toxoplasma antibodies in 3 mothers who had given birth to a child with toxoplasmosis and then a normal child. They found that both types of antibodies were transmitted to the normal infant and almost
disappeared after 4 or 5 months, they suggested when a mother has one child with congenital toxoplasmosis her subsequent children are likely to be normal.

Alexander Macdonald (1950) found out of 250 samples of serum from "normal" pregnant women 13 gave positive complement fixation test for toxoplasma antigen in north west England. Out of 12 children who had both chorioretinitis and cerebral calcification 10 gave positive serological tests for toxoplasmosis, they suggested that such symptomless infection must be kept in mind as infection crosses the placenta.

H.G. Farquhar (1950) reported two cases of congenital toxoplasmosis, he described tetralogy of congenital toxoplasmosis, cerebral calcification, hydrocephalus chorioretinitis and positive serological tests for toxoplasma antibodies he demonstrated antibodies in infected or uninfected children of infected mother.

Jirovee et al (1959) and Langer and Geissler (1960) believe that toxoplasmosis is one of the main infectious cause of repeated abortion in women, other workers believes that women who have congenitally infected child do not have another infected child in subsequent pregnancies, repeated abortion occurs if women developed only an incomplete immunity.
0. Thalhammer (1962) suggested that only when a woman is initially infected with toxoplasma during pregnancy can the infection to her foetus and the infection can get through the placenta only during the second half of pregnancy, so all women at the end of third month of pregnancy should be tested by toxoplasm in skin test, which is cheap and simple. If foetus is in great danger pyrimethamine 25 mg and triple sulphomonamide 3 gm is given daily, which should be continued for 2 to 3 weeks.

It has long been presumed that material infection with T. gondii had to occur during gestation in order to involve the conceptus. Remington (1963) cultured 34 gravida who exhibited serological evidence of chronic toxoplasmosis and whose pregnancy terminated in abortion, still birth or neonatal death. He recovered the organism in two cases of abortion and in one case of neonatal death. This study demonstrates that a gravida does not have to acquire primary infection during gestation to transmit the organism to the conceptus and persistent parasitemia can occur despite high antitoxoplasma antibody level.

Eckerling, Neri and Eylan (1968) studied 40 women with positive serology who previously in 116 pregnancies had produced only 32 surviving infants and after treatment with pyrimethamine and sulphomonamide before pregnancy and with
tetracycline and sulphonamide during pregnancy and these 40 women had 42 pregnancies with 41 healthy children and one abortion. In the light of more recent knowledge that tetracycline is potentially teratogenic it should not be used.

Samuel A., Saxon (1971) suggested that subclinical congenital toxoplasmosis may have an adverse effect on intellectual development, so mothers should be screened for toxoplasmosis and treatment with sulfadiazine and pyrimethamine show no evidence of intellectual impairment.

Andrew Czeizel et al (1971) found toxoplasmosis in 7.7 per thousand pregnancy in Hungary. As toxoplasmosis infection occurring in pregnancy effects only 25% of fetuses the rate of fetal disease was 2 per thousand pregnancies and he found no need for routine screening of disease in all pregnant women in Hungary.

Desmonts Georges et al (1974) studied 378 pregnant women with high initial toxoplasma antibody titres or seroconversion during pregnancy, 183 acquired the infection during pregnancy, a rate of 6.3 per 100 pregnancies. There were 11 abortion, 7 infants were still born toxoplasmosis occurred in 59 of the non aborted offspring. Severe disease was noted only when maternal infection were acquired during the first two trimesters, later resulted in subclinical or no fetal
infection. Treatment with spiramycin during pregnancy reduced overall frequency of fetal infection but not the overt disease. Mothers with antibodies before they become pregnant had no infected infants.

Babili stray Pedersen et al (1975) carried out a serological screening for toxoplasma antibodies among 10,729 pregnant women in the Oslo area and 1007 women in more, frequency of antibody was found to be 12.5% in Oslo area and 13.3% in more, frequency was higher in women living in rural area. Incidence of congenital toxoplasmosis was 2% of all pregnancies. No serological difference was found when women with prior histories of either sporadic and habitual abortion were compared to total group of multigravidae among the Oslo women.

Raux et al (1976) advised that routine serological screening might be worth while where toxoplasmosis is unduly prevalent e.g. in Paris where 75% of all patients in child bearing age have antibodies or in Brussels, where they are present in 53% of antenatal patients and there are two clinically manifested cases of congenital toxoplasmosis in per 1000 births.

J. Cauvrent et al (1976) studied 14 pair of twin with congenital toxoplasmosis illustrated the importance of
placental lesion in determining the extent of fetal involvement and advised screening for toxoplasmosis in pregnancy.

Peter G Beach et al (1978) screened sera from 95,929 pregnant women for antibodies to toxoplasma gondii with indirect hemagglutination test in Oregon, one in every 200 women contracts toxoplasmosis during her pregnancy.

Christopher B Wilson et al (1979) found that most infant born with congenital toxoplasmosis infection are asymptomatic in newborn period but develop neurological, intellectual and auditory deficit later in life, so screening of all pregnant women should be done for toxoplasmosis antibodies.

Wilson et al (1980) found that infection late in pregnancy is usually subclinical at birth but of these children most develop convulsion and other neurological sequelae later in life so all pregnant women should be screened for toxoplasmosis and treatment should be given to positive cases.

Kovar and Harvey et al (1981) found that infection during early pregnancy is most damaging although abortion is not common but when infection occurs during the first trimester one fifth of babies will show full syndrome of chorioretinitis, hydrocephaly and patchy cerebral calcification, associated with impaired vision, convulsion and severe mental handicap. Since neonatal treatment improves the
immediate prognosis in actual disease but does not reduce subsequent ill health and brain damage, the efficacy of antenatal prophylaxis in this way must await long term follow up studies.

Faulen et al (1984) advised repeated testing of susceptible mother for toxoplasma antibodies. It would detect seroconversion due to primary infection or initially high titre would indicate that toxoplasma infection may have occurred early in pregnancy.

Beattie et al (1984) suggested that in Britain, where meat is usually well or over cooked prevalence rate of toxoplasmosis are lower and routine serology would not be cost effective, e.g. in the west of Scotland only 25% of population have antibodies and the seroconversion rate in pregnancy is only 0.2% (Williams et al 1981) compared with 0.4% and 0.67% respectively in French and Belgium studies and the incidence of congenital toxoplasmosis is usually 0.06 per 1000 birth.

Faulen et al (1984) suggested that antenatal drug treatment has some value in preventing transplacental infection when it is known that primary maternal infection has occurred especially in most dangerous early months of pregnancy, he used spiramycin cyclically as a 3 week course with one week interval.
F. Daffas et al (1985) examined 273 pregnant women at risk of infection, incidence of disease is 3% in population. He found that maternal toxoplasmosis in early pregnancy is less opt to be associated with fetal infection than in maternal infection in late pregnancy. If fetal infection occurs however severe disease is more common in those who acquire infection in first half of gestation. This report demonstrates that prenatal diagnosis of fetal infection in pregnancy at risk is useful by identifying maternal antibody. Treatment given was 3 gm spiramycin daily, termination was done in 3 cases inspite of normal ultrasound finding.

J.G. Kappe (1986) did 20 year follow up of patient with congenital toxoplasmosis and found that new lesion continue to develop well after age of 5 years. Screening of women at risk for toxoplasmosis in pregnancy thus seems advisable.

John L Sever (1987) analysed antibody titre for toxoplasmosis in 23,000 pregnant women in Maryland of the 15 pregnancies with raised antibody titre two children had congenital toxoplasmosis and three were still born, doubling in frequency of deafness, 60% increase in microcephaly and 30% increase in low IQ is associated with presence of high maternal antibody to toxoplasma.
Francois Foresties et al (1988) reported a prospective study of 749 documented cases of maternal toxoplasma infection. Infection was diagnosed antenatally in 39 of 42 fetuses, 24 were terminated. 15 mothers were treated with spiramycin. If foetal infection was demonstrated pyrimethamine and either sulfadoxine or sulfadiazine were added to the regimen, only 2 fetuses developed chorioretinitis, remaining were clinically well, so it was concluded that prenatal therapy in women who wish to continue their pregnancies reduces the severity of the manifestation of the disease.

Orellano N et al (1990) studied incidence of toxoplasmosis in pregnant women in various American cities. He found incidence varied from 3-30%.

Roose et al (1993) after screening 2104 women in Germany found 41.6% women were Ig G positive author concluded that screening was both efficacious and cost effective in their propulation.

Portlong, F. et al (1994) estimated high incidence of 0.5 to 1.5% and 30 to 50% of toxoplasmosis in pregnancy. Among the studied 190 women, two third by seroconversion of toxoplasmosis antibody status and one third by rising Ig G titre plus the presence of Ig M, risk of infection was 4%,
17% and 53% respectively in first, second and third trimester, so antenatal screening is cost effective.

Berrebi, A. et al (1994) reported that maternal infection with toxoplasma gondii can cause infection but not in all fetuses. Furthermore appropriate treatment can prevent foetal infection as the parasite does not cross placenta for 4-8 weeks after the onset of maternal infection so termination of pregnancy is no more indicated in cases of maternal toxoplasmosis.

F. Pratilary et al (1995) studied a cohort of 286 antenatal patients for toxoplasma antibodies, 40 were positive, he concluded importance of making diagnosis of toxoplasmosis antenatally in order to limit the number of medical abortion.

Mehta, S. et al (1995) found incidence of toxoplasma seropositivity in the BOH as 24% where as in control group it was 16%. Incidence of abortion was 28%, preterm delivery 20% and incidence of still birth and congenitally malformed fetuses was 25% in patient of BOH. Among the congenital malformations anencephaly, microcephaly, cleft lip and cleft palate were seen.
Soni, I.J.K. et al (1995) found that the frequency of various hazards in Ig M positive cases was abortion 31.8%, preterm birth 22.72%, still birth 13.63% congenital anomaly 4.75% and neonatal birth 4.75%. Thus in pregnant women who were tested Ig M positive, the rate of abortion was tripled and rate of preterm delivery was doubled. It is more common in age group of 24-30 year. 3rd para as compared to 1st and 2nd para. Same incidence among vegetarian and non vegetarian.

Nagar, P. et al (1995) concluded that the incidence of toxoplasmosis was found to be higher in women having repeated abortions, premature births and congenital anomalies. The incidence of repeated abortion in the study was 22%, premature birth was 17.8% and congenital toxoplasmosis was 15%. The maximum age group infected was between 23-27 year. Non vegetarian and patients with contact with pet animals had a definite higher incidence of toxoplasmosis.