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Satyabhama Marandi
Department of Obstetrics and Gynaecology, IMS & SUM Hospital, Siksha O Anusandhan Deemed to be University, K8, Kalinga Nagar, Bhubaneswar, Odisha, India

Tapasi pati
Associate Professor, Dept of Obstetrics and Gynaecology, IMS and SUM Hospital, Bhubaneswar, Odisha, India

Correspondence
Tapasi pati
Associate Professor, Dept of Obstetrics and Gynaecology, IMS and SUM Hospital, Bhubaneswar, Odisha, India

Common infectious diseases in pregnancy and its impact on perinatal outcome: A prospective study

Satyabhama Marandi and Tapasi Pati

Abstract
Introduction: Infectious diseases are a common cause of maternal and perinatal morbidity and mortality especially in tropical and subtropical countries. They encompass viral diseases like viral hepatitis, HIV, rubella, CMV, genital herpes and protozoan diseases like malaria and toxoplasma. Most of these are related to poverty, poor sanitation, parasitic infestations and restricted access to proper health care.
Aims and Objective: To study common infectious diseases in pregnancy and analyse perinatal outcome
Material and Methods: This is a prospective study conducted by taking detailed history of the patients and doing certain investigations like blood hemoglobin, liver function test, coagulation profile, HIV, HBsAg, HCV, TORCH panel, immune chromatography for malaria and ultrasonography for assessment of fetal condition. Neonates were assessed as per its birth weight, fever, irritability, feeding problems, anemia, petechial, jaundice, cyanosis, hepato-splenomegaly and congenital malformations.
Results: Spontaneous abortions were most commonly seen in case of Rubella infection (37.5%) followed by HCV (30%) and malaria (14.7%). HIV infected women were most IUGR fetuses (48%) followed by malaria (34.7%). Most of the intrauterine fetal demise occurred in Toxoplasma gondii infection (44%). Rubella contributed 29.1% of IUFD. Congenital malformations were mostly evident in Rubella infection (20.8%). Most of the perinatal deaths seen in HIV positive women (16%) followed by malaria (6.6%).
Conclusion: Infections in pregnancy are important contributor to maternal and perinatal morbidity and mortality. Awareness, primary prevention, early diagnosis and treatment are required to control seasonal and epidemic diseases such as malaria.

Keywords: infections in pregnancy. perinatal outcome, diagnosis of infectious diseases

Introduction
Though there is 63% fall in maternal mortality over the last 20 years still India contributes 72% of maternal death in South Asia in the year 2013 [1]. Among all the causes of maternal mortality and morbidity, pregnancy related infections have the highest case fatality ratio [2]. Several factors responsible for infectious disease threat in pregnancy. First, changes in immunity and physiology during pregnancy may make pregnant women more susceptible to or more severely affected by infectious diseases. Second, the effect of infectious diseases on the fetus may be difficult to predict and diagnosis can be challenging. Third, prophylaxis and treatment appropriate for general population might not be appropriate for pregnant women. We focus on the incidence and effects of infectious diseases in pregnancy.

Material and Method
This is a prospective study which evaluated 200 obstetric patients who underwent antenatal checkup in OPD or admitted to the labor room of Obstetrics and Gynecology department of Institute of medical science and SUM hospital, Bhubaneswar, Odisha during the period from October 2016 to September 2018. Detailed history of the patients and doing certain investigations like blood hemoglobin, liver function test, coagulation profile, HIV, HBsAg, HCV, TORCH panel, immune chromatography for malaria, ultrasonography of abdomen and pelvis was done. Pregnant woman with signs of infection but reported to have uterine anomalies, active or suspected gynecological disorder, clinical evidence of cervical incompetence and any major surgery involving uterus and cervix were excluded from this study. Neonates were assessed as per its birth weight, fever, irritability, feeding problems, anemia, petechial, jaundice, cyanosis, hepato-splenomegaly and congenital malformations.

Observation
Total 200 cases were studied out of which 75 (37.5%) were Malaria, 25 (12.5%) cases of HIV,

HBV and toxoplasmosis each. Rest includes 24(12%) cases of Rubella, 10 (5%) cases of HCV, 9(4.5%) cases of CMV and 7(3.5%) cases of Genital herpes (Table. 1).

Table 1: Percentage distribution of cases

Disease	No. of cases	Percentage (%)
Malaria	75	37.5
HIV	25	12.5
HBV	25	12.5
HCV	10	5
Toxoplasma	25	12.5
Rubella	24	12
CMV	9	4.5
Genital herpes	7	3.5
Total	200	100

Table 2: Distribution of age (years)

Disease	17-23	24-30	>31	Total
Malaria	34	27	14	75
HIV	13	7	5	25
HBV	15	5	5	25
HCV	7	2	1	10
Toxoplasma	14	7	4	25
Rubella	13	7	4	24
CMV	5	2	2	9
Genital herpes	3	3	1	7

Table 3: Parity distribution

Disease	Nulli	Primi	Multi	Total
Malaria	25	22	28	75
HIV	5	10	5	25
HBV	3	12	10	25
HCV	3	4	3	10
Toxoplasma	12	8	5	25
Rubella	12	7	5	24
CMV	5	2	2	9
Genital Herpes	3	2	2	7

The study revealed that all the infections are common in third trimester except for Genital herpes which has no preponderance for any trimester (Table 4). As per table 5, the infections were most common in lower socio-economic group.

Table 4: Distribution of disease according to gestational age (weeks)

Disease	<12	13-28	29-40	Total
Malaria	5	6	64	75
HIV	1	4	20	25
HBV	3	7	15	25
HCV	1	2	7	10
Toxoplasma	5	7	13	25
Rubella	3	7	10	24
CMV	3	2	4	9
Genital Herpes	2	2	3	7

Table 5: Distribution according to socioeconomic status

Disease	Low	Average	High	Total
Malaria	40	30	5	75
HIV	13	7	5	25
HBV	15	7	3	25
HCV	7	2	1	10
Toxoplasma	15	7	3	25
Rubella	13	8	3	24
CMV	6	2	1	9
Genital herpes	5	1	1	7

Table.6 depicts the perinatal outcome in different infections. Further analyzing the outcome we found that spontaneous abortions were most commonly seen in case of Rubella infection (37.5%) followed by HCV (30%) and malaria (14.7%). Preterm delivery is a common complication of malaria (36%) followed by CMV infection (33.3%). HIV infected women were most IUGR fetuses (48%) followed by malaria (34.7%). Most of the intrauterine fetal demise occurred in Toxoplasma gondii infection (44%). Rubella contributed 29.1% of IUFD. There is no intrauterine deaths in HIV, HBV, HCV, CMV infections. Congenital malformations were mostly evident in Rubella infection (20.8%). Most of the perinatal deaths seen in HIV positive women (16%) followed by malaria (6.6%). Premature rupture of membrane is commonly encountered in CMV infection (44.4%) and HBV infected women (12%).

Table 6: Percentage of perinatal outcome in different infection

Outcome	Malaria		HIV		HBV		HCV		Toxoplasma		Rubella		CMV		Genital herpes	
	No.	%	No	%	No	%	No	%	No	%	No.	%	No.	%	No.	%
Spontaneous abortion	11	14.7	1	4	0	0	3	30	7	28	9	37.5	0	0	2	28.5
Preterm delivery	27	36	6	24	0	0	3	30	3	12	0	0	3	33.3	1	14.2
IUGR	26	34.7	12	48	2	8	0	0	0	0	0	0	0	0	1	14.2
IUFD	4	5.3	0	0	0	0	0	0	11	44	7	29.1	0	0	2	28.5
Congenital malformation	0	0	0	0	0	0	0	0	2	8	5	20.8	0	0	0	0
Perinatal death	5	6.6	4	16	0	0	0	0	2	8	0	0	0	0	0	0
PROM	2	2.7	2	8	3	12	0	0	0	0	0	0	4	44.4	0	0
Normal	0	0	0	0	20	80	4	40	0	0	3	12.5	2	22.3	1	14
TOTAL	75	100	25	100	25	100	10	100	25	100	24	100	9	100	7	100

Not much of adverse effect was found in case of HBV infection. 20 out of 25 cases (80%) were normal babies (fig.1). Only 2 (8%) cases of IUGR and 3 (12%) cases of premature rupture of membranes were associated with HBV infection.

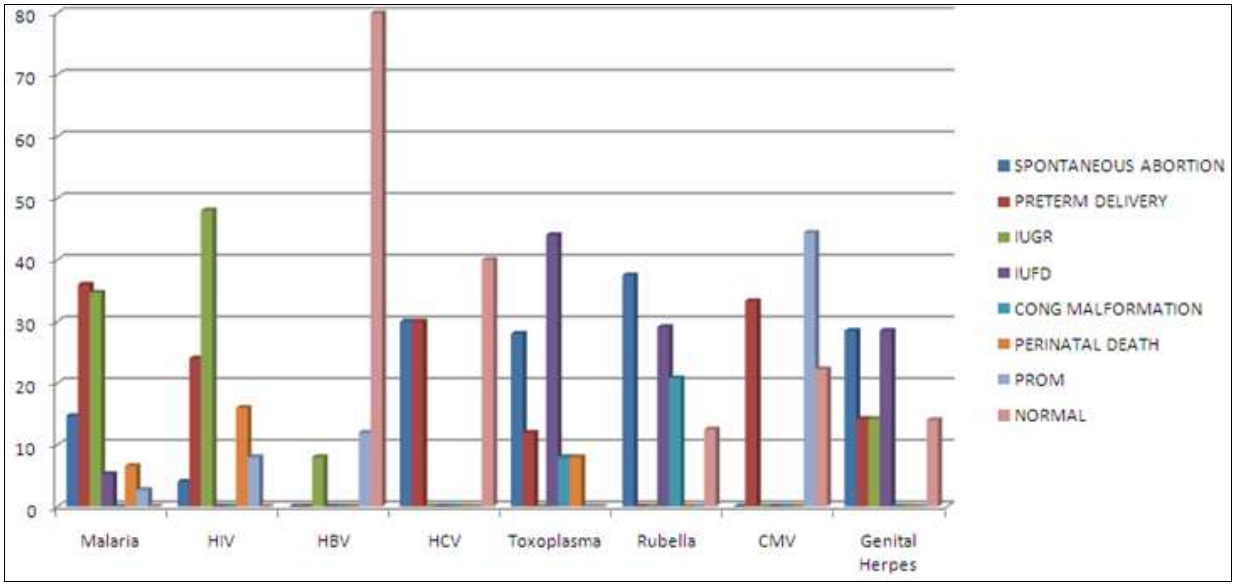

Fig 1: Perinatal outcome in different infections

Discussion

Infectious diseases are common cause of maternal and perinatal morbidity and mortality especially in tropical and subtropical countries. They encompass viral diseases like viral hepatitis, HIV, rubella, CMV, genital herpes and protozoan diseases like malaria and toxoplasma. Most of these are related to poverty, poor sanitation, parasitic infestations and restricted access to proper health care.

Amongst all infectious diseases HIV has assumed to be alarming in our country. Mother to infant transmission is the primary means by which young children become infected with HIV Type 1. In HBV infection, intrapartum transmission occurs if the mother has acute infection in late pregnancy or is a chronic carrier of HBe antigen. Toxoplasma, Rubella, CMV infection during pregnancy leads to fetal infection and subsequent fetal death or congenital anomalies in the fetus. Malaria acquired during pregnancy is one of the major causes of maternal morbidity and poor birth outcome in tropical countries like India.

Keeping this in view a prospective study was undertaken to record and analyze common infectious diseases complicating pregnancy, their prevalence, their effect on pregnancy and overall perinatal outcome. The diseases covered in this study included: Malaria, HIV, Hepatitis, Toxoplasma, Rubella, CMV, Genital herpes.

Pregnant women in malaria – endemic area are at increased risk of becoming infected with parasite. The increased incidence and severity may occur specially in primiparous women. Although parasite density is highest in non-immune women during their first pregnancy, even a previously immune women can become more susceptible to malaria infection during pregnancy [2]. It is widely accepted that malaria has a negative effect on the outcome of pregnancy and perinatal loss can be as high as 60-70% [3, 4, 5, 6]. In our study, malaria (37.5%) remains the most important cause of perinatal mortality (34%). Primiparae are more likely to suffer from adverse maternal outcomes due to severe anemia and cardiac failure during labor, whereas multiparous women have milder maternal symptoms but suffer from disproportionately high perinatal morbidity and mortality due to innate immunity and placental sequestration of malarial parasites [7, 8, 9]. Malaria infection can cause maternal anemia, low birth weight and possibly abortion and still births [10]. The mean birth weight of the infants born by mothers with placental malaria is reduced by 55-310grams [11-18]. A meta-analysis study confirmed that malaria is associated with a more than two fold risk for still birth, regardless of parity [19].

Toxoplasma gondii is a parasite that infects human primarily through ingestion of infected raw or undercooked meat and less frequently, by exposure to infected cat faces. This intracellular pathogen can be transmitted transplacentally to the fetus. A cross-sectional study of 2242 women in Brazil showed that previous pregnancy was a risk factor for toxoplasmosis [20]. In a follow up study, it was confirmed that pregnant women who were sero negative for Toxoplasma were more than twice as likely as non-pregnant women to seroconvert [21]. Our institution witnessed 25(12.5%) cases toxoplasmosis with 2 (8%) perinatal deaths. Congenital malformations like hydrocephalous, ventriculomegaly and intracranial calcification can be evident in toxoplasma infection in utero. Amniotic fluid PCR has now become the optimal method to detect the exposure of the fetus to T. Gondii infection. A combination of perinatal screening by ultrasonography and amniotic fluid PCR has led to a correct diagnosis of congenital toxoplasmosis in 98% cases [22]. Maternal to fetal transmission is dependent on the time in pregnancy that maternal infection is acquired. The mean transmission rate in pregnancy is 29% to 35% [22, 23]. Although spiramycin appears to reduce the risk of transmission by almost 60%, it is not effective to treat an infected fetus after 18 weeks of gestation [24]. The later in pregnancy the maternal infection is acquired, the more frequently the parasites are transmitted to fetus and the higher incidence of congenital toxoplasmosis [25, 26]. However, the earlier in pregnancy the fetus is infected, the more severe is the clinical condition in the infant. We encounter 2 perinatal deaths, 7 (28%) spontaneous abortions, 3(12%). Preterm deliveries, 11(44%) intrauterine deaths, 2(8%) congenital malformed fetuses. All fetuses out of 25 were affected.

Perinatal transmission of HIV infection occurs if untreated. The benefits of antiretroviral treatment (ART) in decreasing mother to child transmission (MTCT) of HIV infection is well established [27]. In India, the program for Prevention of mother to child transmission (PMTCT) of HIV was launched in the year 2002. With effect from 2014, India adopted the World health organization (WHO) instigated option of B + for prevention of MTCT of HIV. There were few perinatal deaths (4 out of 25) in HIV women in our study. The possible explanation is that being

a privately owned institute, there is few HIV+ve women registered in our hospital because the Indian government provides highly active antiretroviral therapy (HAART) in an attempt to suppress viral load below detection to minimize MTCT of HIV and all delivery services to those mothers free of cost at government hospitals.

Hepatitis in pregnancy is commonly associated with abortions, premature delivery. HBV infection in India is of intermediate endemicity with nearly 4% of the population being chronic hepatitis B virus carrier that is about 40 million people. HBsAg is not believed to cross placental barrier but is usually acquired at birth or shortly thereafter. Chronic HBV infection during pregnancy is an important opportunity to interrupt perinatal transmission of HBV. In one study, HBV and HCV infected women had higher rates of preterm deliveries, premature rupture of membranes, abruption placenta, congenital malformations and low birth weight infants. In our study, HBV infection doesn't appear to increase the fetal morbidity or mortality rather HCV caused 3 spontaneous abortion and 3 preterm deliveries out of 10 cases.

The Rubella virus is one of the most teratogenic agent for humans affecting fetal growth and leading to congenital rubella syndrome (CRS). The first report regarding fetal consequences of maternal rubella infection was published by Gregg in 1941. The frequency of fetal affection is 80-90% when maternal infection occurs during first trimester, 54% at 13-14 weeks and 25% at the end of second trimester (Miler *et al*, 1982). As clinical diagnosis of rubella is unreliable, serological tests like detection of rubella specific IgM and IgG antibody (four fold rise in titre) and more recently PCR are needed [28]. There is more risk of congenital anomalies like hydrocephalous, cardiac anomalies and amniotic fluid alternation. As there is no in utero treatment available for infected fetus, women should be counseled about the possible risk of vertical transmission and offered pregnancy termination especially if primary infection occurs prior to 10 weeks of gestation. In our study, spontaneous abortion (37.5%) and fetal wastage (29.1%) were most commonly seen in rubella infection.

Cytomegalovirus (CMV) infection usually doesn't cause any long term health consequences in an healthy individual. Pregnant women who are at infected with CMV rarely have symptoms but rather their developing fetus in utero may be at risk of congenital CMV disease. There are two different types of CMV infection - primary CMV and recurrent CMV infection. Primary infection can cause more serious problems in pregnancy than recurrent infections can. Most common complications include low amniotic fluid level, IUGR and hydrocephalous. We didn't encounter any such complications in our study.

The risk of herpes transmission to fetus are greatest when a women acquires a new infection (primary genital herpes) in the third trimester particularly within six weeks of delivery as viral shedding may persist and the baby is likely to be born before the development of protective maternal antibodies. Rarely congenital herpes may occur as a result of trans placental intrauterine infection. Few reports suggest that the skin, eyes, and central nervous system may be affected and there may be IUGR or fetal deaths. Around 2% of women acquire genital herpes infection in pregnancy and most of the maternal infections are asymptomatic or unrecognized [29].

Conclusion

Infections in pregnancy are important contributor to maternal and perinatal morbidity and mortality. Awareness, primary prevention, early diagnosis and treatment are required to control seasonal and epidemic diseases such as malaria which still remained the major cause of perinatal mortality.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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