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Seroprevalence of Cytomegalovirus and Rubella among Women seeking Antenatal care and the implications of Socio-demographic, Obstetric and Clinical determinants

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ABSTRACT

Vertical transmission of maternal infections of Cytomegalovirus (CMV) and Rubella virus (RV) have serious fetal and neonatal outcomes. A cross sectional study was conducted with 471 pregnant women attending antenatal clinics in Chennai city to determine the seroprevalence of CMV and RV and the contributing factors. Serum samples of the study population were screened for the IgM and IgG antiviral antibodies by ELISA. The seroprevalence of CMV and RV were 87% and 56% respectively. While the rate of past (IgG) and primary (IgM) infections were higher for RV, the CMV caused more active infections (IgM+IgG). Significant sociodemographic characteristics associated with CMV and RV infections were pregnancy in advanced age (OR=0.916, CI=0.712-1.861, P=0.028), low education level (OR=1.792, CI=1.212-2.996, P=0.039) and living in rural areas (OR=2.314, CI=1.492-3.237, P=0.028). The infection during first pregnancy (OR=0.827, CI=0.581-0.996, P=0.036), 1st trimester (OR=1.496, CI=0.998-1.853, P=0.015) and high rate of miscarriage (OR=2.958, CI=2.212-3.826, P=0.032) were the recorded obstetric risk factors. Clinical features significantly attributed to the infections were abnormal BMI (OR=0.861, CI=0.468-1.221, P=0.028), abnormal hemoglobin level (OR=0.862, CI=0.542-0.972, P=0.044) and history of jaundice (OR=0.383, CI=0.128-0.539, P=0.021). The study suggested the need for regular serological surveillance, vaccination and awareness education to prevent the infections caused by CMV and RV.

INTRODUCTION

Congenital infections are considered as a major threat to the antenatal health care as they are often implicated with the teratogenegis in the developing fetus. These infections occur due to the vertical transmission of maternal infection from the mother to the fetus. Certain blood-borne pathogenic agents such as Cytomegalovirus (CMV), Herpes Simplex viruses (HSV), Rubella virus (RV), Varicella Zoster virus (VZV) and Venezuelan equine encephalitis virus are frequently known to cause infections *in utero* (Erfanianahmadpoor et al., 2014). Among these agents, the CMV and RV are reportedly highly pathogenic and associated with the risks of congenital defects, spontaneous abortion and fetal mortality (Teklu et al., 2016; Hunsperger et al., 2024).

CMV is a member of Herpesviridae family and known to undergo latency in reticuloendothelial cells after causing a primary infection. The main reservoir of CMV is man and it can be transmitted by both direct and indirect methods (Karabulut et al., 2011). Generally, the sexual behavior of the mother and the contact with infected children are recognized as the common sources of infection. In the infected individuals, it occurs in saliva, oropharyngeal and endocervical secretions, tears, breast milk, urine, vaginal secretions and sperm. The blood products and organs infected with CMV are considered highly contagious (Barlinn et al., 2018; Maleghemi et al., 2025). When reactivated, the latent virus can cause secondary infections and morbidity especially in immunocompromised patients (Ozdemir et al., 2024). Complications due to CMV infections vary according to the gestational age. The rate of infection is usually moderate in the first trimester (36%) and gradually increase during the second (77.6%) and last trimester (77.6%) of pregnancy (Leruez-Ville et al., 2013; Mamvura et al., 2015). However, severe complications of the disease may occur if the infection of the mother occurs before 20 weeks of the fetal growth (Khan et al., 2025).

Research studies have reported that the CMV is a leading cause of congenital infections during the perinatal periods which leads to teratogenic effects such as severe neurological impairment, permanent loss of hearing and vision (Moosavy, 2011; Almakki et al., 2024). The CMV often causes asymptomatic infections and has a global spread with the seroprevalence of antiviral antibodies

ranging 53-97% in different geographical regions (Vueba et al., 2022).

The Rubella virus (RV) is transmitted by air-borne route through respiratory droplets and is usually associated with mild or self-limited infections (Teklu et al., 2016). The viremia associated with the maternal infection of RV facilitates trans-placental transmission of the virus which leads to the infection of the growing fetus. Onset of infection during the first trimester is associated with hostile neonatal complications often referred to as congenital rubella syndrome (CRS) (Leruez-Ville et al., 2013). The morbidities include heart disease, deafness, cataract, delayed growth, etc. (Mamvura et al., 2015; Maleghemi et al., 2025). Owing to the high tropism shown by the virus towards the fetal tissues, more severe adverse effects of the fetal infection occur during the period of organogenesis. Some reports claim that the defects may also occur during the second trimester (Radoi et al., 2024).

By virtue of introduction of rubella vaccine in the immunization schedule of the countries by the initiative of WHO in the year 2000, there is overall decline of the infection worldwide. However, in some African countries high incidence of the infection amounting to 95.3% have been reported (Erfanianahmadpoor et al., 2014; Papa et al., 2024).

Since these two viruses viz., CMV and RV are widespread in occurrence and incriminated with devastating effects on the fetus and the neonates, their early detection would help assuring proper gynecological and obstetric care. Surveillance of the women under antenatal care plays a vital part in the prevention of vertical transmission of these viruses. The studies concerning the seroprevalence of these viruses among the pregnant women are scanty in Indian context. Therefore, this study was conducted to elucidate the seroprevalence of CMV and RV among the pregnant women of different gestation age and attributing risk factors of their infections.

MATERIALS AND METHODS

Study population

A cross-sectional study was conducted during the period of October 2012 to March 2013 with the pregnant women attending five antenatal clinics located at different area of Chennai city, India. Among the women seeking antenatal care, a total of 427 pregnant woment volunteered for the study. Informed consent was obtained from each women volunteer though explaining the objectives of the research. Using a structured questionnaire, the enrolled women were interviewed to gather information on sociodemographic characteristics, clinical and obstetrical features. The body mass index (BMI) of each volunteer was calculated through measuring the height and weight. The study was reviewed and approved by the Research Ethics committee of the Department of Microbiology of Asan Memorial College, Chennai.

Specimen collection and laboratory screening

From each volunteer of the study population, 5 mL of blood was collected. The blood samples were allowed to clot and centrifuged at 2500 rpm for 10 minutes to separate the sera. Each serum sample was designated with an identification code and stored at -20ºC until use. The serological testing of the serum samples was carried out using the Enzyme-linked immunosorbent assay (ELISA) technique. Commercial diagnostic kits (ADALTIS, USA) were used for the detection of IgM and IgG antibodies to CMV and RV. Quantitative estimation of antibody levels was expressed as IU/mL through calculating the absorbance values recorded by using ELISA reader. Procedures were followed according the manufacturer's instructions. The cut-off index of negative vs. positive controls were determined as follows: anti-CMV IgG < 0.6 vs. > 1.0 IU/mL; anti-CMV IgM < 0.8 vs. > 1.0 IU/mL; anti-RV IgG < 9.0 vs. > 10.0 IU/mL and anti-RV IgM < 0.9 vs. > 1.0 IU/mL.

Subsequent to detection of profile of antibodies, the sero-status of the women was categorized into three categories: "Past infection" [IgG(+)/IgM(−)], "Active infection" [IgG(+)/IgM(+)],and "Primary infection" [IgG(−)/IgM(+)].

Statistics

The data were prepared on Excel sheets and analyzed using SPSS version 20. The categorical and quantitative variables were subjected to exploratory analysis and expressed as percentages (±SD). Sub category variables were assessed by Chi-square analysis and corresponding p-values are presented. Logistic regression of the effect of the attributing risk factors on the seroprevalence of CMV and RV was studied using multivariate and bivariate analysis. Statistical significance was determined if the value of each data is set as $p < 0.05$.

RESULTS

Seroprevalence of CMV and RV

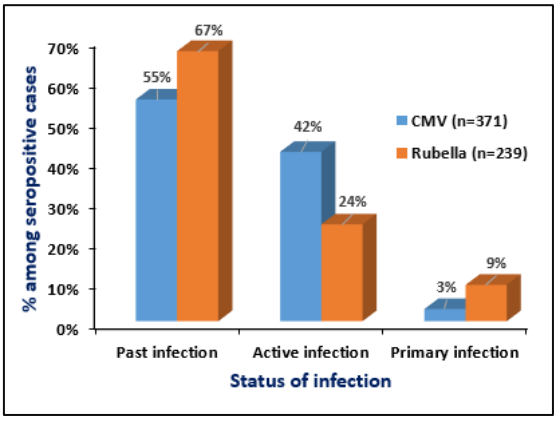

Figure 1. Serostatus of CMV and RV infections among pregnant women

Out of the 427 serum samples tested, the seroprevalences of CMV and RV were observed to be 87% (371/427) and 56% (239 /427) respectively. Category-wise serostatus of the infections of CMV and RV are presented in the figure 1. While the past and primary infections were high for RV (67 and 9%), higher preponderance of active infection was associated with CMV (42%) than RV (24%).

Sociodemographic characteristics vs. seropositivity

Tables 1 and 2 represent the sociodemographic characteristics of the pregnant women who showed seropositivities to CMV and RV respectively. In both the seropositive cases, the advancing age (≥35 years) was observed to be statistically significant. Similarly, the low level of education was significantly associated with the seropositivities to both CMV and RV. None of the occupational categories were observed to impact the infections by these two viruses. While the residence of living was insignificant for RV, the seropositivity to CMV was significantly associated with the women hailing from the residences of rural area.

Table 1. Sociodemographic characteristics of CMV seropositive pregnant women

Variable	CMV seropositive group (N=371)			
	n (%)	OR	95% CI	*P* value

Age				
≤ 25 years	157 (42)	0.968	0.561-1.113	0.921
26-34 years	123 (33)	0.654	0.129-0.943	0.843
≥35 years	91 (25)	1.532	0.852-2.365	0.043*
Education level				
Low	86 (23)	1.792	1.212-2.996	0.039*
Primary	172 (46)	0.891	0.294-1.118	0.924
Secondary	113 (31)	0.923	0.671-1.432	0.178
Occupation				
Housewife	188 (51)	0.728	0.169-0.941	0.067
Farmer	54 (15)	0.637	0.116-0.837	0.893
Employee	129 (35)	0.886	0.591-1.383	1.002
Residence				
Urban	193 (52)	0.573	0.164-0.829	0.724
Peripheral	84 (23)	0.965	0.628-1.212	0.995
Rural	94 (25)	2.314	1.492-3.237	0.028*

Table 2. Sociodemographic characteristics of RV seropositive pregnant women

Variable	Rubella seropositive group (N=239)			
	n (%)	OR	95% CI	*P* value
Age				
≤ 25 years	127 (53)	1.757	1.121-2.894	0.891
26-34 years	64 (27)	0.958	0.429-1.368	0.926
≥35 years	48 (20)	0.916	0.712-1.861	0.028*
Education level				
Low	63 (26)	3.211	2.116-3.678	0.047*
Primary	78 (33)	0.952	0.783-1.246	0.094
Secondary	98 (41)	0.786	0.493-0.997	0.841
Occupation				
Housewife	114 (48)	0.459	0.098-0.792	0.198
Farmer	33 (14)	0.613	0.263-0.929	0.515
Employee	92 (38)	0.528	0.121-0.861	0.096
Residence				
Urban	141 (59)	1.263	0.929-2.053	1.024
Peripheral	43 (18)	0.925	0.682-1.493	0.992
Rural	55 (23)	0.897	0.323-1.021	0.845

Obstetric factors vs. seropositivity

Among the obstetric factors analyzed, the parity i.e., the number of pregnancies showed the association with the seropositivities to both CMV and RV (Tables 3 and 4). The prevalences of infections of these two viruses was significantly associated with the women who are pregnant for the first time. With respect to the gestational age, while the seropositivity of CMV was significantly associated with the 3rd trimester, the seropositivity to RV was highly significant with the women of 1st trimester pregnancy. While the miscarriage was insignificant for CMV infections, the higher rate of miscarriage among the RV infected pregnant women was observed to be statistically significant.

Table 3. Obstetric factors associated with seropositivity of CMV in pregnant women

Variable	CMV seropositive group (N=371)			
	n (%)	OR	95% CI	*P* value
Parity				
0	126 (34)	0.827	0.581-0.996	0.036*
1-2	187 (50)	0.995	0.826-1.452	0.925
≥3	58 (16)	2.369	1.896-2.864	1.258
Gestational age				
1st trimester	139 (37)	0.583	0.103-0.793	0.376
2nd trimester	108 (29)	0.687	0.459-0.929	0.287
3rd trimester	124 (33)	0.993	0.623-1.283	0.049*
History of miscarriage				
0	226 (71)	0.196	0.106-0.356	0.112
1	88 (24)	0.782	0.438-0.861	0.125

≥2	57 (20)	0.265	0.106-3.853	0.258

Table 4. Obstetric factors associated with seropositivity of RV in pregnant women

Variable	Rubella seropositive group (N=239)			
	n (%)	OR	95% CI	*P* value
Parity				
0	97 (41)	0.923	0.661-1.326	0.041*
1-2	101 (42)	1.283	0.994-1.829	0.929
≥3	41 (17)	0.569	0.123-0.827	0.386
Gestational age				
1st trimester	112 (51)	1.496	0.998-1.853	0.015*
2nd trimester	73 (31)	1.223	1.095-1.735	0.881
3rd trimester	54 (23)	0.982	0.721-1.282	1.002
History of miscarriage				
0	163 (68)	0.562	0.267-0.781	0.096
1	14 (6)	1.286	0.995-1.894	0.067
≥2	62 (26)	2.958	2.212-3.826	0.032*

Clinical features vs. seropositivity

The abnormal BMI of the pregnant women was significantly associated with the seropositivity to CMV (Table 5) contrary to that of RV (Table 6). While the abnormal hemoglobin level was significant for RV infections, it had no impact on that of CMV. However, the history of jaundice was determined to be a significant risk factor for both CMV and RV seropositive cases.

Table 5. Clinical features vs. seropositivity of CMV in pregnant women

Variable	CMV seropositive group (N=371)			
	n (%)	OR	95% CI	*P* value
Body Mass Index				
Normal	224 (60)	0.293	0.119-0.421	0.094
Abnormal	147 (40)	0.861	0.468-1.221	0.028*
Hemoglobin				
Normal	203 (55)	0.623	0.294-0.868	0.141
Abnormal	168 (45)	0.721	0.526-0.927	0.082
History of jaundice				
Yes	154 (42)	0.383	0.128-0.539	0.021*
No	217 (58)	0.299	0.138-0.351	0.184

Table 6. Clinical features vs. seropositivity of RV in pregnant women

Variable	Rubella seropositive group (N=239)			
	n (%)	OR	95% CI	*P* value
Body Mass Index				
Normal	107 (45)	0.265	0.119-0.625	0.099
Abnormal	132 (55)	0.884	0.562-1.388	0.986
Hemoglobin				
Normal	142 (59)	1.269	0.989-1.675	0.392
Abnormal	97 (41)	0.862	0.542-0.972	0.044*
History of jaundice				
Yes	98 (41)	0.897	0.583-1.029	0.044*
No	141 (59)	0.569	0.281-8.636	0.721

Note: Abbreviations on the tables 1-6: OR, Odds ratio; CI, confidence interval; *Statistically significant ($p < 0.05$)

DISCUSSION

The antenatal care aims at proper monitoring of the maternal and fetal health. It includes not only the supervision of nutrition, but also the detection and prevention of any agents that cause teratogenic or detrimental effects on the fetus. With respect to the blood-borne pathogens such as Cytomegaovirus (CMV) and Rubella virus (RV) that cause maternal infections, care of highest priority to prevent their vertical transmission. Periodical serological testing and analysis of associated risk factors of infections constitute the surveillance to prevent and control the fetal mortality and neonatal morbidities.

The congenital infections caused by CMV constitute the major cause of mortality and morbidity. It is associated with the complications ranging 0.2-2.6% among the total number of births worldwide (Mamvura et al., 2015). Reports indicate that out the total primary material infections, 40% of cases lead to fetal infections. The present study recorded a seroprevalence of 87% of CMV infections among the pregnant women tested. Similar rates of prevalence have been reported by earlier studies in different countries such as Gambia, Egypt, Benin and in South East Asia with a range of 87-97.2% (Erfanianahmadpoor et al., 2014). The higher prevalence of this virus in general population has been reported by many studies. This may be attributed to its widespread nature and transmission through multiple routes such as direct contact, air borne route and vertical transfer. Since CMV is a blood borne pathogen, infections with HIV could predispose its higher

prevalence in African countries (Maleghemi et al., 2025). However, the European countries show low prevalence of this virus. With respect the to the serostatus of CMV infection among the study population, higher past infections (55%) and active infections (42%) indicate its latent characteristics and periodical reactivation (Figure 1). Factors such as maternal sexual activity, breast feeding and neonatal care contribute to the epidemiology of CMV (Hamdan et al., 2011; Papa et al., 2024).

The seroprevalence of RV among the study population was 56% which is similar to the range of prevalences (50-68%) reported from Nigeria, Sudan and Democratic Republic of Congo. In certain African countries substantial prevalence (88.6%) of RV has been reported. The variations of prevalence may be attributed to the prenatal endemicity of the virus, sampling and screening methods for evaluation (Kahraman Kilbas et al., 2025). Another important factor is the vaccination against the RV, which is not uniformly adopted in the immunization schedules of different countries. The higher rate of past infections, i.e., the presence of anti-IgG RV antibodies, among the pregnant women of the present study (Figure 1) may be due to the vaccination taken by the individuals on voluntary basis.

The multivariate analysis of sociodemographic characteristics (Tables 1 and 2) indicated that the pregnancy in advanced age (≥35 years) is significantly associated with both CMV (OR=1.532, CI=0.852-2.365, P=0.043) and RV infections (OR=0.916, CI=0.712-1.861, P=0.028). Grada et al. (2024) explained that pregnancy in late age might compromise the immunity to these viruses and constitute a risk factor for infections. The significant association of seopositivities of CMV (OR=1.792, CI=1.212-2.996, P=0.039) and RV infections (OR=3.211, CI=2.116-3.678, P=0.047) with low level education indicate the lack of awareness on hygienic practices that are essential for the prevention of infections by these viruses. Similar finding has been reported by Maleghemi et al. (2025). The pregnant women hailing from rural areas such as villages showed significant prevalence of CMV infection (OR=2.314, CI=1.492-3.237, P=0.028). Due to the lack of proper sanitary practices and poor living conditions, the populations of the rural areas are, in general, prone to infectious diseases. The CMV, due to its multiple route of transmission, could be present in wide range of sources and infected susceptible individuals.

The logistic regression of impact of obstetric factors (Tables 3 and 4) on the seroprevalences demonstrated that the first pregnancy is significantly associated with the CMV (OR=0.827, CI=0.581-0.996, P=0.036) and RV (OR=0.923, CI=0.661-1.326, P=0.041) infections. Since the first pregnancy is critical for obstetric care, the vertical transmission of maternal infections might compromise the health status of the fetus (Barlinn et al., 2018). Even though the association of CMV with the 3rd trimester pregnancy is indicated as significant (OR=0.993, CI=0.623-1.283, P=0.049), the infection of RV during the 1st trimester makes it highly significant (OR=1.496, CI=0.998-1.853, P=0.015). Vueba et al. (2022) have stated that the congenital infection of RV during the early stages of pregnancy enables the virus to infect the immature fetus due to higher affinity to the emerging tissues. The virulence of the RV virus is evident from the finding of its significant association with higher rates of miscarriage among the pregnant women of our study (OR=2.958, CI=2.212-3.826, P=0.032). Concomitant finding has been recorded in the studies of Abdulali (2023).

The study of clinical features of the enrolled population by bivariate analysis showed that the abnormal BMI is significantly associated with the CMV infection (OR=0.861, CI=0.468-1.221, P=0.028). This may be due to comorbid conditions such as obesity and diabetes which might compromise the immunity to the virus leading to higher rate of infection during the pregnancy (Ozdemir et al., 2024). Another important observation of the present study is the abnormal hemoglobin level as the risk factor for RV infection (OR=0.862, CI=0.542-0.972, P=0.044). In general, proper antenatal care is given to counter the alterations of hemoglobin levels during the pregnancy. Hunsperger et al. (2024) have explained that abnormally low levels of hemoglobin indicate the deficiency of iron and associated electrolyte concentrations in the body and eventual susceptibility to infections. The previous history of jaundice has been significantly associated with the infections of both CMV (OR=0.383, CI=0.128-0.539, P=0.021) and RV (OR=0.897, CI=0.583-1.029, P=0.044). This may be attributed to the defects in the liver caused by many factors including the blood borne Hepatitis viruses such as HBV and HCV (Aliyu et al., 2024). Since these viruses are reportedly sexually transmitted, the maternal sexual behavior can be viewed as a risk factor for their infections. Similarly, the CMV and RV infections also indicate the possibility of direct mucosal transmission, history of jaundice could be a considerable risk factor (Yeshwondm et al., 2016; Almakki et al., 2024).

The vertical transmission of maternal infections of CMV and RV, if unchecked, could lead to severe adverse effects during the fetal development and later neonatal growth. Therefore, it is essential to reduce the circulation of these viruses in the pregnant women which needs awareness of the contributing risk factors, vaccination (in the case of RV) and regular clinical and laboratory testing of the pregnant women. The health care planners and providers need to play critical roles for the regular surveillance of these viruses in this risk group for ensuring reliable antenatal care.

CONCLUSION

The seroprevalences of CMV and RV depends on the geographical endemicity, hygienic practices and vaccination status. Higher prevalence of CMV (87%) may be due to its ability of establishing latency and periodical reactivation. The affinity of RV to fetal tissues causes its higher preponderance over CMV (9% vs 3%) in causing the primary infection in pregnant women. Pregnancy in advanced age, low education level and living in rural areas could be the contributing factors of CMV and RV infections due to the lack of awareness of prevention of infections. Infections during the first child bearing and first trimester of gestation may constitute the significant risk factors for antenatal care. Higher rates of miscarriage might be attributed to the virulent nature of the RV. Abnormal BMI and hemoglobin levels indicate the association of comorbid conditions and nutritional deficiency which might compromise the immunity to both CMV and RV. History of jaundice relate the risk factors such as blood borne transmission and maternal sexual behavior attributed to the infections by these two viruses.

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