



Brief Report

Prevalence of Congenital Toxoplasmosis and Congenital Rubella among Suspected Infants in Baghdad

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ABSTRACT

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Congenital toxoplasmosis (CT) and congenital rubella (CR) infections are well-known causes potentially leading to devastating consequences. This report aims to address the prevalence of each of these infections among suspected infants in a pediatric hospital in Baghdad.

The study sample includes 120 blood samples of suspected infants consulting Al-Alwyia pediatric teaching hospital over one year. This report represents an extension of a previous article published in Al-Kindy College Medical Journal KCMJ about cytomegalovirus infection (CMV). Using the enzyme-linked immunosorbent assay (ELISA) method, the results show that 5.8% and 5% were positive for specific IgM antibodies for rubella and toxoplasmosis respectively. Results also show that CMV is more common than CT and CR.

Although results reported one case of co-existence of IgM antibodies for both CMV and rubella, there was a significant association of negative CMV IgG and IgM results with positive rubella results; and negative rubella results with CMV IgG and IgM results.

Conclusions: This short brief addressed the prevalence of CT and CR in Baghdad. A novel finding identified in this brief is the association of the prevalence of CR active infection with negative past and negative recent CMV infections, and the association of prevalence of CMV active and past infections with negative CR infection.

Recommendations: The study recommends increased awareness, early diagnosis and treatment for congenital infection, and consolidation of coverage of the rubella vaccine for children and girls at premarital age.

Introduction

Measuring disease frequency (prevalence or incidence) is among the most fundamental measures in epidemiology to understand the burden on the health and social care system at a particular time that influences decision-making about what public health interventions are required (1).

TORCH infections (Toxoplasmosis, Other infections, Rubella, Cytomegalovirus, and Herpes simplex virus) are a group of

congenitally acquired infections that cause significant morbidity and mortality in neonates. Identifying infants with such infections by serum TORCH antibody testing is crucial for the detection of these congenital infections (2), of which the IgM antibody detection is considered the primary approach for active infection (3). Congenital rubella (CR) and congenital toxoplasmosis (CT) are well-known congenital infections which can lead to variable manifestations

including birth defects, and other serious consequences such as severe neurological sequelae and mental retardation (3,4), CT can be treatable when diagnosed at an early time (4), while CR is a mainly preventable disease through vaccination.

Congenital cytomegalovirus (CMV) can share similar manifestations to other TORCH infections such as toxoplasmosis and rubella (6). A TORCH screen panel of tests for detecting antibodies for *Toxoplasma gondii*, rubella, CMV, and Herpes Simplex Virus (HSV), are usually used in a variety of assay formats including the enzyme-linked immunosorbent assay (ELISA), rapid assays, and bead-based assays antibodies (Abs) for these pathogens concomitantly. Reactivity for the IgM, but not IgG, usually indicates a current infection, while IgG without IgM suggests a past infection (7,8)

During our work on the manuscript (Prevalence of congenital cytomegalovirus among suspected infants in Baghdad 2019-2020) published in Al-Kindy College Medical Journal (KCMJ) Vol. 18 No. 1 at 2022 (9), we came across the prevalence of CT and CR among the study sample of patients. As far as the prevalence of CT and CR in Baghdad is scarce, it is crucial to address this information and shed light on it.

Subjects and Methods

According to this cohort study, blood samples were taken for 120 infants consulting Al-Alwyia pediatric teaching hospital suspected infants over one year (from 1st of October 2019 to 1st of October 2020). Males constitute 54.17% and the 1-3 months age group infants constitute 29.17% of the sample as shown in table 1. Criteria for inclusion included the presence of any of the following: jaundice, hepatosplenomegaly, rash, congenital malformations, hearing or ophthalmological abnormalities, and various CNS manifestations like convulsions or delayed milestones.

Serum samples were tested for rubella and toxoplasma-specific IgM Abs in addition to CMV-IgM and IgG Abs by using commercially available IgM capture ELISA kits (Bioactiva, Germany). According to the manufacturer's instructions, 1.5 - 3 ml of venous blood was obtained, samples were placed in a sterile plain tube, allowed for clotting at room temperature for half an hour, and then centrifuged at 1500 Revolutions per minute (rpm) for 5 minutes. All sera were stored in a repository at -20°C pending testing. The sample was considered positive when the ratio was >1.1, and it was considered negative if <0.9 for both IgG and IgM antibodies. Initial equivocal results were repeated in 10-14 days. CMV-IgM negative results were furtherly classified according to the presence or absence of CMV-specific IgG Abs.

The study was approved by the Al-Risafa research ethical committee and by the Ministry of Health- Iraq as part of the Al-Risafa Health Directorate research plan for 2020 which authorized the researchers to study these congenital infections in infancy. Furthermore, this paper is part of the currently implemented TORCH project for the identification of causative microorganisms attributed to congenital anomalies. This project is supported, approved, and sponsored by the public health directorate/ MOH-Iraq. Furthermore, the Training and Planning Directorate / MOH-Iraq and the Research Ethical Committee/ Baghdad Al-Risafa Health Directorate approved

our research study and plan as part of the 2020 research plan. Parents' verbal approvals were obtained as far as patients involved did require routine investigations that did not involve further interventions like surgery and drugs. The statistical data analysis approaches used to analyze and assess the results of the study were done under the application of the statistical package (SPSS) version (22.0).

Results

The prevalence rates of CR and CT were 5.8% and 5% respectively. There is a significant association between rubella IgM positive results and CMV (IgG & IgM) negative results. the CMV IgM positive and negative results are associated positively with Rubella IgM negative results (with a P value of 0.028).

Table 1: Gender and age distribution of whole sample

1-Gender	No .	%
Males	65	54.17
Females	55	45.83
Total	120	100
2- Age (month)	No .	%
< 1	27	22.5
1-3	35	29.17
4-6	25	20.83
7-9	16	13.33
10-12	17	14.17
Total	120	100

Table 2: Prevalence of Rubella -IgM and toxoplasmosis-IgM antibodies during infancy distributed according to CMV IgG +ve , CMV IgM +ve, and CMV -ve with comparison significance

Finding	No. & %	CMV IgG +ve result	CMV IgM +ve result	CMV (IgG & IgM) -ve result	Total	C.S. P-value *
Rubella IgM -ve	No. 65 % 98.5%	19	95.0%	29	113	C.C. = 0.237
Rubella IgM +ve	No. 1 % 1.5%	1	5.0%	5	7	P=0.028 S
Total	No. 66 % 100	20	100	34	120	
toxoplasma IgM -ve	No. 62 % 93.9%	20	100%	32	114	C.C. = 0.102
toxoplasma IgM +ve	No. 4 % 6.10%	0	0.0%	2	6	P=0.531 NS
Total	No. 66 % 100	20	100	34	120	

Discussion

IgM Abs for rubella in our study was detected among 5.8% of infants with suspected congenital infection (table 2 and figure 1). Up to our knowledge, there was no available registered data regarding the occurrence of CR in Iraq previously (10). Reported acquired rubella cases in Iraq flared up to 197 cases in 2021. Reported cases were 10, 9, and 21 in 2020, 2019, and, 2018 respectively (11). Acquired rubella is a mild childhood illness. It has a high risk on susceptible pregnant mothers that may lead to abortions or congenital infections.

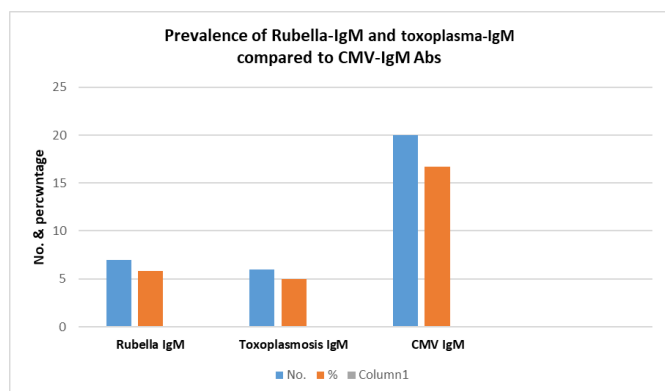


Figure 1: Prevalence of Rubella-IgM and toxoplasma-IgM compared to CMV-IgM Abs

In 2019 the coverage for the 1st dose of the rubella-containing vaccine in Iraq was 86%, this figure was increased to 92.33 in 2020. Unfortunately, it has decreased again to 84.05% in 2021 (12). As of December 2018, 168 out of 194 countries had introduced rubella vaccine programs and global coverage was estimated at 69%. These programs include vaccinating girls (aged 10-14 years) in addition to early childhood vaccinations (13).

CR is still highly encountered in many developing countries. For example, rubella-specific IgM Abs were detected in 21.2%, of suspected infants from 2016-to 2018 in India (14). In Sudan, CR cases were attributed to 7.6 % of suspected infants in 2012 (15). Differences in the prevalence of CR are related to differences in the prevalence of rubella among pregnant mothers who can catch the infection if not vaccinated.

Toxoplasma-IgM Positive Abs in this study were found to constitute 5% of infants suspected to have a congenital infection (table 2 & figure 1). 15.9% of suspected children < 5 years of age were found to have toxoplasma-IgM Abs according to a study done in Al- Alwyia pediatric hospital in Baghdad in 2005 (16). This high figure is particularly contributed to the fact that diagnosis of CT after the first year of life is confounded by the possibility of the child acquiring infection in the postnatal period (17).

According to a meta-analysis published in 2019, toxoplasma-IgM was positive in 4.10% of Iranian neonates suspected to have CT while toxoplasma-IgM was positive in 3.02% of suspected Mexican children according to another meta-analysis published in 2012 (18,19).

This paper as far as we know is the 1st to identify the prevalence of CR and the 2nd to identify CT among suspected infants in Iraq. A previous study done in Al-Nasiriya- Iraq tested IgG antibodies for TORCH infections (but did not test IgM prevalence) among newborn infants suffering prolonged neonatal jaundice (20). These IgG isotype antibodies reflect maternal antibodies passed transplacentally to the fetus rather than active neonatal infection (21). The prevalence of rubella- IgM and toxoplasma -IgM among our findings were lower than the CMV- IgM prevalence (figure 1 & table 2).

Among suspected cases, IgM Ab estimates were 16.7% (9), 5.8%, and 5% for CMV, rubella and toxoplasmosis respectively. These findings are in concordance with other studies elsewhere as far as the transmission rate for CMV is higher for CMV infection (22). we found one case of coexistence of CMV and rubella-specific IgM antibodies. IgM multi-positive results by ELISA don't

necessarily indicate co-infections of multiple TORCH pathogens. These can be caused by cross-reactions between antibodies and antigens during immunoassays (3). A true IgM multi-positive results for CMV and rubella-specific IgM antibodies indicating co infections are rare instead (3,23).

CMV IgM positive and CMV IgG results were found to be significantly associated with rubella IgM negative results in 19 out of 20 and 65 out of 66 CMV IgM positive and negative results respectively. CMV IgG positive results were found to be significantly associated with rubella IgM negative results in 19 out of 20 of CMV IgM positive results on the other hand CMV (IgG & IgM) negative results were found to be significantly associated with rubella IgM positive results in 5 out of 7 of rubella IgM positive results (P=0.028). This novel finding identified in this brief might denote a cross-protection between rubella and CMV. This cross-protection (up to our knowledge) was not yet mentioned in the literature although the heterologous immunity and cross-reactivity of adaptive immune was traced back to the first vaccine by Edward Jenner in the late seventeenth century when he used a cowpox virus to immunize against smallpox infection. In general, heterologous immunity is relatively common within closely related species but can also be seen with unrelated agents (24). In accordance with our finding, CMV carriage was associated with delayed IgG decay over time after live attenuated rubella vaccine (p = 0.034) (25). The CMV infection was also found to prevent reactivation of EBV in humans (26).

Furthermore, murine CMV was found to cross-protect against lymphocytic choriomeningitis virus (LCMV) and Pichinde virus (PV) with different efficiencies (27). As information about cross-protection and heterogeneous immunity between CMV and rubella viruses is scarce, further studies are suggested.

Conclusion

It is concluded that CT and CR infections are next to CMV among suspected congenitally infants. We recommend increasing coverage of rubella vaccination for girls at premarital age and in the pediatric vaccination program. Pregnant women should be screened routinely and frequently for TORCH infections. Furthermore increased awareness of these congenital infections is recommended for early diagnosis and treatment for these infections.

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Conflict of Interest

No conflict of interest

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