Clinical and Experimental Obstetrics & Gynecology

Clin. Exp. Obstet. Gynecol. **2023**; 50(12): 279
https://doi.org/10.31083/j.ceog5012279

Original Research

Impact of COVID-19 on Cytomegalovirus Immunoglobulin M Antibody Index

Masatoki Kaneko[1,2,*,†], Junsuke Muraoka[1,†], Li Yang[1], Shuichi Tokunaga[1], Toshio Minematsu[3]

[1]Department of Obstetrics and Gynecology, Faculty of Medicine, University of Miyazaki, 889-1692 Miyazaki, Japan
[2]Graduate School of Nursing Science, University of Miyazaki, 889-1692 Miyazaki, Japan
[3]Research Institute for Disease Control, Aisenkai Nichinan Hospital, 887-0034 Nichinan, Japan
*Correspondence: mkaneko@med.miyazaki-u.ac.jp (Masatoki Kaneko)
[†]These authors contributed equally.
Academic Editor: Michael H. Dahan
Submitted: 30 June 2023 Revised: 27 August 2023 Accepted: 7 September 2023 Published: 29 December 2023

Abstract

Background: Coronavirus disease 2019 (COVID-19) influenced the prevalence of other infectious diseases, including congenital cytomegalovirus (CMV) infection. However, the effect of COVID-19 on antibody titers has not been reported. This study aimed to explore the influence of COVID-19 on levels of CMV immunoglobulin M (IgM) in pregnant women. **Methods**: This cross-sectional study included pregnant women who visited the University Hospital due to CMV IgM positivity during the 7th and 8th waves of COVID-19. Data, including maternal characteristics, history of COVID-19, CMV immunoglobulin G (IgG) and IgM index, and IgG avidity index (AI) were collected. Chemiluminescent immunoassay was performed to measure levels of IgG and IgM. Polymerase chain reaction using neonatal urine was performed to confirm congenital infection. **Results**: Of the 89 pregnant women, 36 (40%) (low IgG AI: n = 10; high IgG AI: n = 26) contracted COVID-19. Among 21 women with low IgG AI, 9 (false IgM positive: n = 8; primary infection: n = 1) had an IgG AI of 0. Among the eight women with false IgM positivity, six (75%) contracted COVID-19. The IgM index of pregnant women with false IgM positivity was 12.6 $\pm$ 10.9. Meanwhile, the CMV IgM index of pregnant women with false IgM positivity in the non-COVID-19-infected group was 1.7 $\pm$ 0.5. When the IgM indices of women who contracted (n = 36) and did not contract (n = 53) COVID-19 were compared, the IgM index of infected women (4.4 $\pm$ 5.7) was higher than those of non-infected women (2.7 $\pm$ 3.0) (p = 0.01). Regarding IgM and IgG AI, multiple logistic regression analysis revealed that there were no significantly different variables between the two groups. **Conclusions**: High prevalence of false IgM positivity was observed among women who contracted COVID-19. The IgM index of pregnant women with false IgM positivity was high. Caution should be exercised in interpreting CMV IgM indices in pregnant women with a history of COVID-19.

Keywords: COVID-19; cytomegalovirus; chemiluminescent immunoassay; immunoglobulin M; pregnancy

1. Introduction

In 2019, a severe outbreak of coronavirus disease 2019 (COVID-19) caused by the severe acute respiratory syndrome-coronavirus 2 (SARS-CoV-2) occurred worldwide. During the outbreak, long-term quarantine and distancing were recommended to protect vulnerable individuals and prevent infection [1]. Preventive measures led to social isolation and impaired interpersonal communication, thereby resulting in feelings of discomfort, anxiety, panic, anger, resentment, and despair as well as an increase in the rates of domestic violence [2]. Moreover, infection control measures impacted not only mental health but also the spread of other infectious disease. In 2020–2022, usual outbreaks of seasonal influenza and rubella did not occur in Japan [3]. Moreover, respiratory syncytial virus infection was not prevalent among infants in 2020 in Japan; however, it was reported in 2021 and 2022 [3].

Cytomegalovirus (CMV) is the most common virus that causes morbidity and mortality in congenitally infected fetuses and newborns, resulting in a broad range of disabilities (e.g., sensorineural hearing loss, visual impairment, and motor and cognitive deficits) [4]. The prevalence rate of congenital CMV infection ranges from 0.2% to 2.0% in newborns. However, 10%–15% of newborns with CMV infection are symptomatic [4,5]. In Japan, the prevalence of congenital CMV infection in newborns is 0.31% [6]. However, the prevalence of congenital CMV infection during the COVID-19 outbreak significantly decreased in several areas [7,8].

The number of patients who contracted COVID-19 remarkably increased during the 7th and 8th waves of the COVID-19 pandemic (i.e., between July 6, 2022 and January 24, 2023) in Japan compared with other waves. Similarly, several pregnant women contracted COVID-19 during these periods. Along with the number of pregnant women who contracted the disease, we experienced an in-

crease in the number of pregnant women referred due to CMV immunoglobulin M (IgM) positivity during the 7th and 8th waves. Acute and chronic viral infections can induce long-term immunological effects. After recovery from natural acute measles infection, there is a marked reduction in humoral immunity and increased susceptibility to nonmeasles infections [9]. The Bacillus Calmette–Guérin (BCG) live vaccine can reduce allcause mortality in infants due to its pathogen nonspecific effect [10,11]. Hence, it is thought that BCG "train" innate immune cells such as monocytes and their progenitors [10,11]. However, the effect of COVID-19 on the immune response to CMV has not been reported. Thus, this study aimed to clarify the influence of COVID-19 on CMV IgM levels in pregnant women.

2. Patients and Methods

Pregnant women who underwent routine maternal serum screening at primary clinics during the first maternal health checkup were enrolled to the study. Blood samples to detect CMV IgM and immunoglobulin G (IgG) were obtained and subjected to routine maternal serum screening. Blood samples for anti-CMV antibody screening were centrifuged at 10,000 rpm for 15 min and analyzed by chemiluminescent immunoassay (CLIA) using Architect® i2000SR (Abbott Diagnostics, Chicago, IL, USA) analyzer in SRL laboratory. The Architect™ CMV IgM and IgG (Abbott Medical Japan LCC, Tokyo, Japan) were used to measure levels of antibodies. In CLIA, specimens are reacted with magnetic particles on which the CMV antigen was immobilized. After washing off the unreacted material, hydrogen peroxide water and sodium hydroxide were added, and the chemiluminescence of acridinium was measured as emission intensity; the validity of CLIA has been confirmed [12,13]. Cutoff values for CMV IgG and IgM levels were 6.0 AU/mL and 1.0 (index), respectively, and were interpreted according to the manufacturer's instructions. The CMV IgM index was automatically calculated by the instrument as the ratio of the luminescence intensity of the sample to the cutoff value (average luminescence intensity of calibrator $\times$ 1.00) from the measurement results of the sample and control. The cutoff value was stored as a calibration result for each reagent lot. Maternal serum samples were routinely stored in a refrigerator for 1 week prior to further use.

After evaluating CMV IgM positivity, pregnant women were referred to the University Hospital between July 6, 2022 and January 24, 2023 for clinical consultation; those who provided informed consent were enrolled in this study. The same maternal sera used to measure CMV IgG and IgM levels were used to measure the CMV IgG avidity index (AI) at Aisenkai Nichinan Hospital (Miyazaki, Japan). IgG avidity assay was conducted as previously described [4], with slight modifications. The Enzygnost anti-CMV enzyme-linked immunosorbent assay kit (Siemens Healthcare Diagnosis, Tokyo, Japan) was used for the analysis. Maternal information, including age, medical complications, obstetrical history, history of COVID-19 before routine maternal serum screening, and severity of COVID-19, were obtained from medical charts. COVID-19 was diagnosed by SARS-CoV-2 polymerase chain reaction (PCR) on nasopharyngeal swabs performed at the health center. Patients were judged to be severely ill when they received respiratory management.

Amniocentesis at approximately 20 weeks of gestation was offered to pregnant women to confirm fetal infection using PCR, which was performed within 2 weeks for all neonates born to pregnant women who were CMV IgM positive.

Negativity for IgG, positivity for IgM, and an IgG AI of 0 after repeated serological tests at appropriate intervals represented nonspecific immunoreactions to CMV IgM.

Statistical Analysis

Between-group differences were assessed using the Mann–Whitney U-test, χ^2 analysis, or Fisher's exact test. Differences among four groups were assessed using the Kruskal–Wallis test. A $p < 0.05$ indicated statistical significance.

Multivariable logistic regression analysis was performed to identify independent predictive factors. Only predictive variables with a $p < 0.2$ in the univariate analysis were entered into a logistic regression model. A stepwise forward procedure using the likelihood ratio test was used in the multivariable logistic regression analysis. Variables with $p < 0.05$ in multivariable logistic regression were determined as independent predicative factors.

Statistical analysis was performed using SPSS software program for Windows, version 22 (IBM SPSS Statistics, Tokyo, Japan). Data are presented as the mean $\pm$ standard deviation.

3. Results

Overall, 89 pregnant women who were referred to the University Hospital during the study period were included in this study; among them, 36 contracted COVID-19. The characteristics of the women according to a history of COVID-19 infection are shown in Table 1. CMV IgM levels were significantly higher in the COVID-19-infected group versus the noninfected group ($p = 0.01$). Two independent factors, namely the IgM index and IgG AI, were entered into the multivariate model; there were no significantly different variables (IgM; $p = 0.18$, odds ratio: 1.095, 95% confidence interval: 0.959–1.25, IgG AI; $p = 0.45$, odds ratio: 0.993, 95% confidence interval: 0.974–1.012). The number of pregnant women with a low IgG AI was similar in both groups. One case of congenital CMV infection was observed in the noninfected group. The characteristics of pregnant women with a low IgG AI according to a history of COVID-19 infection are shown in Table 2. There were no significant differences in CMV IgG levels,

Table 1. Characteristics of pregnant women according to COVID-19 history.

	COVID-19-infected group (n = 36)	non-COVID-19-infected group (n = 53)	*p* value
Age (years)	31.5 ± 4.5	30.4 ± 5.7	0.37
Primipara (n)	12	20	0.67
Timing of serological test (weeks)	12.5 ± 4.2	12.7 ± 4.6	0.71
CMV IgG (AU/mL)	145.0 ± 86.6	143.1 ± 74.5	0.66
CMV IgM (index)	4.4 ± 5.7	2.7 ± 3.0	0.01
IgG avidity index	42.4 ± 24.5	49.2 ± 24.2	0.10
Low IgG avidity index (n)	10	11	n.s.
High IgG avidity index (n)	27	42	n.s.
Congenital CMV infection (n)	0	1	n.s.

COVID-19, coronavirus disease 2019; n.s., not significant; CMV, cytomegalovirus; IgG, immunoglobulin G; IgM, immunoglobulin M.

Table 2. Characteristics of pregnant women with low avidity index according to COVID-19 history.

	COVID-19-infected group (n = 10)	non-COVID-19-infected group (n = 11)	*p* value
Age (years)	29.8 ± 3.5	29.5 ± 5.5	0.65
Primipara (n)	4	4	1
Timing of serological test (weeks)	14.1 ± 7.4	18.0 ± 7.5	0.06
CMV IgG (AU/mL)	32.9 ± 44.7	52.7 ± 54.7	0.31
CMV IgM (index)	8.4 ± 9.8	3.2 ± 4.1	0.09
IgG avidity index	10.3 ± 14.1	11.0 ± 14.6	0.76
CMV IgM false positivity (n)	6	2	

IgM indices, and IgG AI between the groups. Nine pregnant women had an IgG AI of 0. Among them, eight had false-positive CMV IgM results; six (75%) and two (25%) in the COVID-19-infected and noninfected groups, respectively. The remaining case in the noninfected group was considered as primary maternal infection (CMV IgG, 37.1 AU/mL; IgM, 2.58). Overall, there was no significant difference in the frequency of false IgM positivity between the COVID-19-infected (6/36) and noninfected (2/53) groups ($p = 0.06$). In pregnant women with low IgG AI, there was no significant difference in the frequency of false IgM positivity between the COVID-19-infected (6/10) and noninfected (2/11) groups ($p = 0.08$). The CMV IgM index in pregnant women with false IgM positivity in the COVID-19 infected group was 12.6 ± 10.9, whereas that in the noninfected group was 1.7 ± 0.5.

The characteristics of pregnant women with a high IgG AI according to a history of COVID-19 infection are shown in Table 3. There were no significant differences in CMV IgG levels, IgM levels, and IgG AI between the groups.

Among the four groups (i.e., COVID-19-infected with low IgG AI, noninfected with low IgG AI, COVID-19-infected with high IgG AI, and noninfected with high IgG AI), the IgM index was not significantly different ($p = 0.06$).

There was a case of an infant with a congenital CMV infection in the noninfection group. In this case, primary maternal CMV infection was suspected due to CMV IgM positivity (12.4) and low IgG AI (18%) at 12 weeks of gestation. Notably, the patient did not contract COVID-19. At 38 weeks of gestation, the patient delivered a male newborn that weighed 2770 g. The neonate had signs of CMV infection (liver dysfunction and thrombocytopenia) at birth and developed mild hearing impairment in the left ear.

4. Discussion

In this study, we showed that the prevalence of false positivity for CMV IgM in pregnant women with history of COVID-19 was high. Moreover, the CMV IgM index in pregnant women with false IgM positivity was high.

The presence of CMV-specific IgM is useful in detecting pregnancies at high-risk for vertical CMV transmission. However, there is no global consensus regarding maternal serum screening for CMV infection due to the lack of established screening protocols for detecting congenital infection, effective measures for intrauterine treatment, and vaccine [4]. Additionally, immunoassay may potentially cause false-positive or false-negative results, which may cause clinical problems. In CMV maternal serological screening, pregnant women with CMV IgM positivity and low IgG AI could be considered as being high-risk for vertical transmission. Misinterpretations can cause unnecessary anxiety to pregnant women, which may potentially influence their decision to abort the fetus [14]. In this study, false CMV IgM positivity was confirmed by IgG negativity, IgM positivity, and an IgG AI of 0 after repeated serological tests at appropriate intervals. As a result, false CMV IgM positivity did not cause clinical problems.

Table 3. Characteristics of pregnant women with high avidity index according to COVID-19 history.

	COVID-19-infected group (n = 26)	non-COVID-19-infected group (n = 42)	*p* value
Age (years)	32.1 ± 4.8	30.6 ± 5.9	0.33
Primipara (n)	8	16	0.54
Timing of serological test (weeks)	11.9 ± 1.9	11.3 ± 1.7	0.10
CMV IgG (AU/mL)	188.1 ± 53.2	166.8 ± 59.5	0.09
CMV IgM (index)	2.9 ± 1.5	2.6 ± 2.6	0.08
IgG avidity index	54.8 ± 14.2	59.3 ± 14.0	0.11

In this study, 60% of pregnant women with low IgG avidity in the COVID-19-infected group showed false CMV IgM positivity, although there was no statistically significant difference in the frequency of pregnant women with false positivity between the infected and noninfected groups. Moreover, the IgM index in these pregnant women was extremely high. COVID-19 may activate the immune system to produce a variety of antibodies, which may include crossreactive antibodies against CMV. Vandervore *et al.* [15] revealed a high prevalence of false-positive herpes simplex (HSV) IgM serology and significant elevation of HSV IgM indices as measured by a CLIA-based serology assay (Liaison® XL diagnostics platform, DiaSorin, Salugia, Vercelli, Italy) for herpes simplex in patients with COVID-19. Additionally, they found the presence of an interfering factor in these patients through interference elimination tests [15]. Hence, they concluded that the false-positive results for HSV was caused by the direct binding of SARS-CoV-2 IgM antibodies to surface-modified polystyrene microparticles [15]. COVID-19 infection reportedly produces false-positive reactions in dengue serologic immunoassays [16]. Although CLIA reported false-positive results, the validity of this assay has been proven in a previous Japanese report. Kumada *et al.* [12] reported that repeatability studies using three different control and serum samples showed that simultaneous repeatability ranged from coefficient of variation (CV) 0% to 3.6% for Architect™ CMV IgG and from 0% to 6.3% for Architect™ CMV IgM. Meanwhile, the daily difference repeatability ranged from 0% to 7.6% for Architect™ CMV IgG and from 0% to 5.9% for Architect™ CMV IgM [12]. In a sensitivity test for Architect™ CMV IgG or IgM using a seroconversion panel, CMV IgG and IgM were positive on days 33 and 29, respectively. Meanwhile, in a sensitivity test for a commercial enzyme immunoassay kit (Denka Seiken, Tokyo, Japan), CMV IgG and IgM were positive on days 43 and 29, respectively [12]. In a correlation test between Architect™ CMV IgG and a commercial enzyme immunoassay kit, the overall agreement rate was 99%, the positive agreement rate was 100%, and the negative agreement rate was 96.7% [12].

Acute Parvovirus B19 infection may also cause antibody crossreactivity with the Epstein–Barr virus IgM or HSV IgM in assays performed based on the Liaison platform (DiaSorin, Salugia, Vercelli, Italy) [17]. Crossreaction have also been observed in other immunoassays. Gong *et al.* [18] reported that Architect rubella IgM, CMV IgM, and antihepatitis C virus (HCV) showed cross-reactivity with other disease-specific antibodies. Thus, antibodies from other infections may serve as interfering substances. However, no false positives of the listed antigens were found in this study.

Interferences in the immunoassay include rheumatoid factor or other autoantibodies, heterophilic antibodies, human antianimal antibodies, albumin, complement, lysozyme, fibrinogen, and paraproteins [19]. As these interferences can cause nonspecific reactions, the presence or absence of these factors should be recognized in interpreting the results. In this study, no participant had concomitant autoimmune diseases. According to the instructions of the manufacturer, when negative and positive samples containing endogenous interfering substances were measured and compared to each control sample, no effect was found on the measurement results.

The limitation of this study was that we did not measure SARS-CoV-2 IgM and IgG levels due to its retrospective design. Pregnant women were diagnosed with COVID-19 by SARS-CoV-2 PCR on nasopharyngeal swabs performed at the health center before maternal serological testing. Accordingly, we could not investigate which antibody caused interference that resulted in false CMV IgM positivity and the correlation between CMV IgM index and SARS-CoV-2 IgM and IgG titers. As Japanese law required a 2-week quarantine period during the COVID-19 pandemic, all pregnant women underwent serological testing at least 2 weeks after contract COVID-19. Thus, as all pregnant women already likely experienced seroconversion at the time of the first visit at obstetric facilities, the SARS-CoV-2 IgG was presumed to be an interfering substance.

In this study, we did not include the case of vertical transmission among the COVID-19-infected group. Thus, it remains unknown whether COVID-19 contributes to vertical transmission of CMV. Yamada *et al.* [20] showed that a threatened premature delivery was a risk factor for congenital CMV infection in pregnant women with nonprimary CMV infection. Although there are several factors that contribute to premature delivery, the inflammatory response can also cause premature delivery. They speculate that bacterial infection at the fetomaternal interface, such as at the decidua and villi, activated the latent virus in the uterus

[20]. It may be possible that inflammation of the decidua and villi due to SARS-CoV-2 could trigger vertical transmission of CMV. In such cases, CMV IgM may be positive with SARS-CoV-2 infection. However, it remains unknown whether severely affected individuals with COVID-19 who develop cytokine storm are also infected with CMV or have CMV reactivation. A major primary defense mechanism of the innate immune response against viruses is the complement system [21,22]. Although the main function of the complement system is to protect the host from invading viruses, its overactivation plays a role in COVID-19 pathogenesis. The complement system can be activated via three different pathways (i.e., classical, lectin, and alternative). Overactivation of the complement system via the lectin pathway caused a cytokine storm and vasculitis in patients with severe COVID-19 [23,24]. Thus, CMV, which latently infects vascular endothelial and macrophage-based cells, can be reactivated by COVID-19. Further investigations are warranted to elucidate this process.

The CMV IgM index was significantly higher in pregnant women with a history of COVID-19 compared with those without a history of COVID-19. However, there were no significantly different variables between the groups when CMV IgM and IgG AI were included into the multivariate model. The results indicate that the IgG AI was a confounding factor for the CMV IgM index. Moreover, the reason that the standard deviation of the CMV IgM index was higher than the point estimate (mean) for all subgroups was also due to a confounding factor.

5. Conclusions

High prevalence of false IgM positivity was observed among women who contracted COVID-19. The IgM index of pregnant women with IgM false positivity was high. Caution should be exercised in interpreting CMV IgM indices in pregnant women with a history of COVID-19.

Abbreviations

AI, avidity index; COVID-19, coronavirus disease 2019; CMV, cytomegalovirus; IgG, immunoglobulin G; IgM, immunoglobulin M; SARS-CoV-2, severe acute respiratory syndrome-coronavirus 2.

Availability of Data and Materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Author Contributions

MK and JM designed the research study. MK, JM and LY performed the research. JM and ST collected the data. TM and MK analyzed the data. MK and JM wrote the manuscript. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

This study was conducted in accordance with the guidelines of the Declaration of Helsinki and was approved by the Ethics Committee of the Faculty of Medicine, University of Miyazaki, Miyazaki, Japan (approval number: 0-0829). Informed consent was obtained from all participants involved in the study.

Acknowledgment

We thank Drs. Shunichi Noda, Ikuo Nakayama and Hiroyuki Watanabe for their cooperation in collecting the data.

Funding

This work was supported by JSPS KAKENHI, grant number JP21K09452.

Conflict of Interest

The authors declare no conflict of interest. Masatoki Kaneko is serving as one of the Guest editors of this journal. Masatoki Kaneko had no involvement in the peer review of this article and has no access to information regarding its peer review. Full responsibility for the editorial process for this article was delegated to Michael H. Dahan.

References

[1] Armitage R, Nellums LB. COVID-19 and the consequences of isolating the elderly. The Lancet. Public health. 2020; 5: e256.

[2] Ren S, Gao R, Chen Y. Fear can be more harmful than the severe acute respiratory syndrome coronavirus 2 in controlling the corona virus disease 2019 epidemic. World Journal of Clinical Cases. 2020; 8: 652–657.

[3] Infectious Disease Weekly Report. 2023. Available at: https://www.niid.go.jp/niid/ja/idwr.html (Accessed: 23 May 2023).

[4] Rawlinson WD, Boppana SB, Fowler KB, Kimberlin DW, Lazzarotto T, Alain S, *et al*. Congenital cytomegalovirus infection in pregnancy and the neonate: consensus recommendations for prevention, diagnosis, and therapy. The Lancet Infectious Diseases. 2017; 17: e177–e188.

[5] Manicklal S, Emery VC, Lazzarotto T, Boppana SB, Gupta RK. The "silent" global burden of congenital cytomegalovirus. Clinical Microbiology Reviews. 2013; 26: 86–102.

[6] Koyano S, Inoue N, Oka A, Moriuchi H, Asano K, Ito Y, *et al*. Screening for congenital cytomegalovirus infection using newborn urine samples collected on filter paper: feasibility and outcomes from a multicenter study. BMJ Open 2011; 1: e000118.

[7] Schleiss MR, Rosendahl S, McCann M, Dollard SC, Lanzieri TM. Assessment of Congenital Cytomegalovirus Prevalence among Newborns in Minnesota during the COVID-19 Pandemic. JAMA Network Open. 2022; 5: e2230020.

[8] Fernandez C, Chasqueira M, Marques A, Rodrigues L, Marçal M, Tuna M, *et al*. Lower prevalence of congenital cytomegalovirus infection in Portugal: possible impact of COVID-19 lockdown? European Journal of Pediatrics. 2022; 181: 1259–1262.

[9] Mina MJ, Kula T, Leng Y, Li M, de Vries RD, Knip M, *et al*. Measles virus infection diminishes preexisting antibodies that offer protection from other pathogens. Science. 2019; 366: 599–606.
[10] Aaby P, Netea MG, Benn CS. Beneficial non-specific effects of live vaccines against COVID-19 and other unrelated infections. The Lancet Infectious Diseases. 2023; 23: e34–e42.
[11] Netea MG, Domínguez-Andrés J, Barreiro LB, Chavakis T, Divangahi M, Fuchs E, *et al*. Defining trained immunity and its role in health and disease. Nature Reviews Immunology. 2020; 20: 375–388.
[12] Kumada H, Tanaka I, Yoshimura T. Evaluation of CMV IgG and IgM by using Automated Chemiluminescent immunoassay system. Japanese Journal of Medicine and Pharmaceutical Science. 2015; 72; 1087–1094. (In Japanese)
[13] Grandjean Lapierre S, Vallieres E, Rabaamad L, Labrecque M, Chartrand C, Renaud C. Evaluation of the Abbott ARCHITECT™ cytomegalovirus IgM/IgG, rubella IgM/IgG, and syphilis treponemal antibodies enzyme immunoassays in a mother and child health center population. Diagnostic Microbiology and Infectious Disease. 2019; 94: 231–235.
[14] Uehara K, Kaneko M, Matsuoka A, Kuroki M, Minematsu T. A cross-sectional study on maternal anxiety levels after cytomegalovirus screening. Journal of Psychosomatic Obstetrics and Gynaecology. 2020; 41: 240–245.
[15] Vandervore L, Van Mieghem E, Nowé V, Schouwers S, Steger C, Abrams P, *et al*. False positive Herpes Simplex IgM serology in COVID-19 patients correlates with SARS-CoV-2 IgM/IgG seropositivity. Diagnostic Microbiology and Infectious Disease. 2022; 103: 115653.
[16] Yan G, Lam LTM, Yan B, Chua YX, Lim AYN, Phang KF, *et al.* Convert COVID-19 and false-positive dengue serology in Singapore. The Lancet. Infectious Diseases, 2020; 20: 536.
[17] Berth M, Bosmans E. Acute Parvovirus B19 infection frequently causes false-positive results in Epstain-Barr virus- and herpes simplex virus-specific immunoglobulin M determinations done on the Liaison platform. Clinical and Vaccine Immunology. 2009; 16: 372–375.
[18] Gong DH, Kim SH, Kim H, Lee A, Han M. Cross-Reactivity of Disease-Specific Antibody Assays for the Detection of Current Infections: with Potentially Interfering Substances of other Infections. Journal of Laboratory Medicine and Quality Assurance. 2022; 44: 40–47.
[19] Ye Q, Zhang T, Lu D. Potential false-positive reasons for SARS-CoV-2 antibody testing and its solution. Journal of Medical Virology. 2021; 93: 4242–4246.
[20] Yamada H, Tanimura K, Tairaku S, Morioka I, Deguchi M, Morizane M, *et al*. Clinical factor associated with congenital cytomegalovirus infection in pregnant women with non-primary infection. Journal of Infection and Chemotherapy. 2018; 24: 702–706.
[21] Schiela B, Bernklau S, Malekshahi Z, Deutschmann D, Koske I, Banki Z, *et al*. Active human complement reduces the zika virus load via formation of the membrane-attack complex. Frontiers in Immunology. 2018; 9: 2177.
[22] Harris SL, Frank I, Vee A, Cohen GH, Eisenberg RJ, Friedman HM. Glycoprotein c of herpes simplex virus type 1 prevents complement-mediated cell lysis and virus neutralization. Journal of Infectious Diseases. 1990; 162: 331–337.
[23] Hurler L, Szilágyi Á, Mescia F, Bergamaschi L, Mező B, Sinkovits G, *et al*. Complement lectin pathway activation is associated with COVID-19 disease severity, independent of MBL2 genotype subgroups. Frontiers in Immunology. 2023; 14: 1162171.
[24] Niederreiter J, Eck C, Ries T, Hartmann A, Märkl B, Büttner-Herold M, *et al.* Complement activation via the lectin and alternative pathway in patients with severe COVID-19. Frontiers in Immunology. 2022; 13: 835156.