Method variation of Cytomegalovirus IgM assays in EQA

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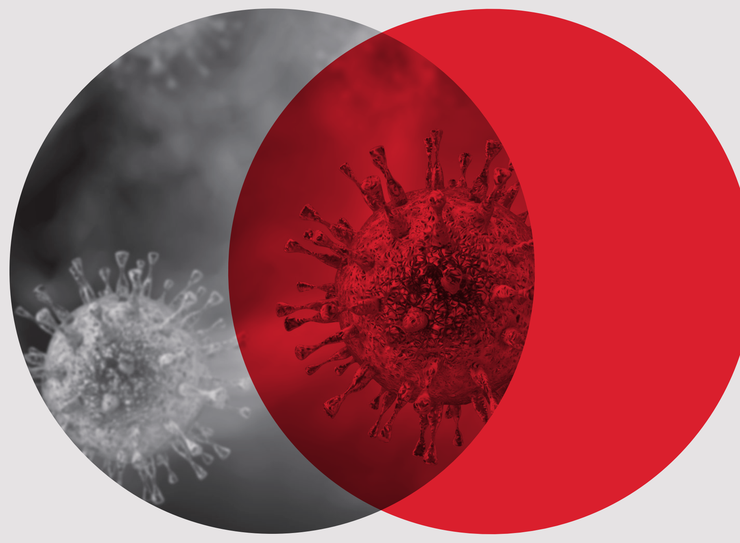

Introduction

Cytomegalovirus (CMV) is a common virus that infects people of all ages. Antenatal serologic screening for CMV is critical to identify pregnancies at higher risk of congenital anomalies. CMV immunoglobulin M (IgM) specificity is known to be poor in detecting primary infections due to viral reactivation or persistence following primary infection. IgG avidity (defined as the strength with which multivalent antibodies bind to multivalent antigens) is recognised as a useful adjunct to IgM in antenatal settings. It is important to note that IgG antibodies with low antigen avidity are present during the early weeks following a primary infection, and increase over time[1,2].

We sought to review the performance of CMV IgM and IgG avidity assays in the RCPAQAP CMV external quality assurance (EQA) program.

Method

A neat, single-source plasma sample (that was IgM positive in the RCPAQAP CMV EQA 2018 survey) was repeated in 2021 and 2022. The qualitative and quantitative results submitted for CMV IgM, IgG and IgG Avidity were extracted from the RCPAQAP database and analysed. Results from four major method groups (Abbott, Diasorin, bioMérieux and Roche) were then compared.

Results

- Over the 4 surveys, the total number of participants submitting CMV IgM results fluctuated between 117 to 124 (average 120) compared to the total number of CMV IgG Avidity entries which varied between 31 to 38 (average 34).
- All methods reported a positive CMV IgG across the 4 surveys.
- Variation in the quantitative and qualitative IgM data across methods was consistently noted, as shown in Figures 1 and 2. Abbott, Diasorin and bioMérieux reported above their respective method cut-offs, Roche reported below. As expected, a similar variation was then reflected in the qualitative interpretations (positive, equivocal, negative, Figure 1).
- Of the 34 laboratories that tested for IgG Avidity in this sample ≥95% consistently reported high, including the 4 method categories reviewed here.

Discussion

CMV IgG avidity is recommended as an additional parameter to assist with differentiating primary infections from non-primary infections in pregnant women[1].

In all surveys, a high CMV avidity was noted, indicating a previous infection (>4 months ago). The IgM reactivity in this sample is likely due to low levels of residual CMV IgM. Therefore, the presence of reactive CMV IgM antibodies should be further investigated by determining the maturity (avidity) of CMV IgG antibodies. However, only 28% of participating laboratories submitted results for both CMV IgM and IgG Avidity.

Conclusion

While this study was limited, it demonstrated the potential to differentiate between a recent primary and a reactivation CMV infection in some settings. Depending on the clinical context, there are recommendations to perform a CMV IgG, IgM and a IgG Avidity profile to aid in identifying recent primary CMV infection in pregnant women[3].

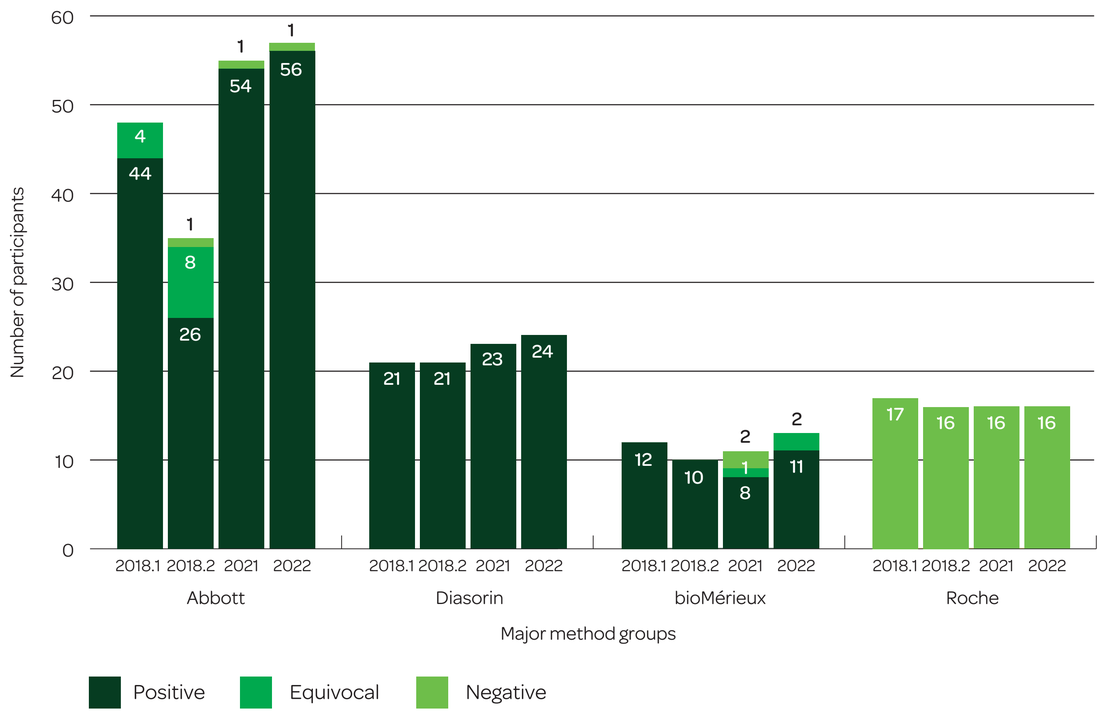

Figure 1. CMV IgM qualitative results received from the major methods groups across 4 surveys. Noting 3 of the 4 groups were predominantly reporting >95% positive results, while Roche reported 100% negative.

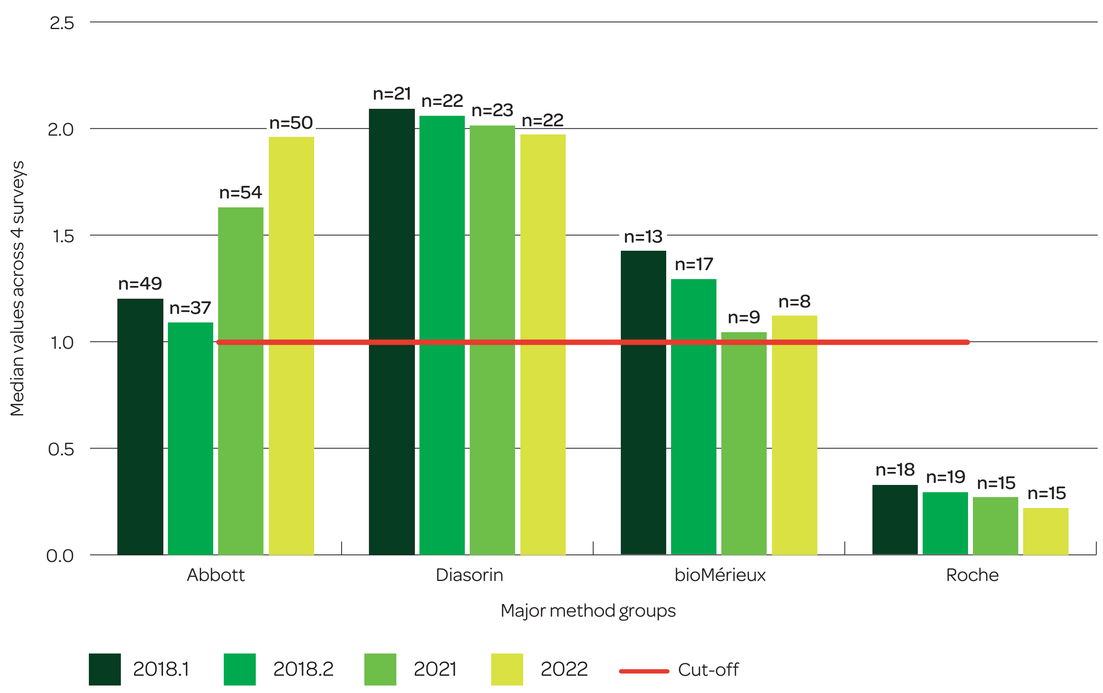

Figure 2. Median values across all 4 surveys from the major method groups compared to a cut-off of 1. Noting 3 of the 4 groups were above or close to the cut-off and Roche were below.

Note* The Diasorin results (cut-off value of 22 U/mL) have been scaled to a comparable ratio value of 1 for illustration purposes.

n= above each column illustrates the number of returned quantitative values for each survey.

References:

1. Iijima, S. (2022) "Pitfalls in the serological evaluation of maternal cytomegalovirus infection as a potential cause of fetal and neonatal involvements: A narrative literature review," Journal of Clinical Medicine, 11(17). Available at: https://doi.org/10.3390/jcm11175006.
2. Gentile, M. et al. (2009) "Measurement of the sensitivity of different commercial assays in the diagnosis of CMV infection in pregnancy," European Journal of Clinical Microbiology & Infectious Diseases, 28(8), pp. 977–981. Available at: https://doi.org/10.1007/s10096-009-0738-0.
3. Prince, H.E. and Lapé-Nixon, M. (2014) "Role of cytomegalovirus (CMV) IGG avidity testing in diagnosing primary CMV infection during pregnancy," Clinical and Vaccine Immunology, 21(10), pp. 1377–1384. Available at: https://doi.org/10.1128/cvi.00487-14.

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