

## Attitude towards screening for congenital cytomegalovirus infection in newborns in Singapore

### Dear Editor,

Cytomegalovirus (CMV) infection is the most common congenital infection.<sup>1</sup> A systematic review that included 77 studies from 36 countries reported that the overall prevalence of CMV was 0.67% in their newborn population.<sup>1</sup> Among newborns with CMV, it was estimated that 15–20% will suffer from potentially deleterious effects including permanent sensorineural hearing loss, intrauterine growth restriction, visual impairment, cerebral palsy and seizure disorders.<sup>2</sup> In fact, congenital CMV (cCMV) is the leading cause of non-genetic sensorineural hearing loss worldwide.<sup>3</sup> While some infected newborns have obvious symptoms, the majority (90%) are asymptomatic, making detection difficult without screening. Asymptomatic newborns remain at risk from long-term sequelae.<sup>4</sup>

Prevalence of cCMV infection in Singapore is unknown,<sup>1</sup> with little publicity about the infection and its complications. A Singapore study reported that only 20% of women who attended a specialist obstetrics and gynaecology clinic in Singapore were aware of CMV and none of their physicians had informed them about it.<sup>5</sup>

Intrauterine CMV infection may occur as primary infection during pregnancy, a reactivation of a previous infection, or an infection caused by a different CMV strain.<sup>6</sup> The transmission risk to the fetus is much higher with primary infection compared with non-primary infection (30–35% versus 1.1–1.7%).<sup>6</sup> Despite this, two-thirds of infection in infants are caused by non-primary maternal infections due to high CMV seroprevalence in adults.<sup>6</sup> In one study, 87% of pregnant women in Singapore was found to be seropositive.<sup>7</sup>

To date, there is no available vaccine for CMV.<sup>8</sup> Infection control measures remain the mainstay to reduce CMV prevalence. In 2015, the International Congenital Cytomegalovirus Recommendations Group convened and recommended consideration to be given for universal neonatal cCMV screening to facilitate early detection and intervention for sensorineural hearing loss and developmental delay.<sup>9</sup> Serologic or virologic CMV screening during antenatal and/or neonatal periods is offered in parts of Europe, the US and Australia.<sup>1,9</sup> However, screening is not discussed nor routinely offered in Asian countries including Singapore.<sup>1</sup> As such, the aim of our study was to evaluate the awareness and attitude of the public towards cCMV

infection and neonatal screening. Information gathered can be used to understand the factors that may guide decision-making if screening was to be implemented.

A questionnaire study was performed between May 2019 and June 2020, on adults of reproductive age attending Otorhinolaryngology, Obstetrics and Gynaecology, and Neonatal and Developmental Medicine clinics at the Singapore General Hospital. The questionnaire was self-administered and anonymous, and structured such that participants would be educated on cCMV infection and newborn screening while being assessed (Appendix A in online Supplementary Material). Data collected were analysed using SPSS Statistics version 25 (IBM Corp, Armonk, US). A *P* value of <0.05 was considered significant.

A total of 709 responses were collected. None of the questionnaires were excluded because of incomplete entry. Despite good awareness of congenital infections (81.4%), there was low awareness of cCMV prevalence (15.7%) and cCMV screening (10.2%). Only 7.4% were aware that diagnosis can only be made before the first 3 weeks of life. There was a significant correlation between the respondent's level of education and awareness of congenital infections. Participants with tertiary education qualification (*n*=542) were more likely to be aware of congenital infections than those with primary (*n*=8, odds ratio [OR] 3.95, 95% confidence interval [CI] 1.099–14.286, *P*=0.036) or secondary education (*n*=62, OR 4.525, 95% CI 2.703–7.576, *P*<0.001).

Few participants (13.7%) were cognisant that babies with cCMV can be asymptomatic at birth. The proportions of respondents who were aware of cCMV causing progressive hearing loss, visual impairment, developmental delay and seizures were 15.6%, 15.6%, 16.7% and 14.4%, respectively. Majority were keen for universal newborn cCMV screening to be offered (589/659, 89.4%). Demographics of participants and their attitude towards cCMV testing are shown in Appendix B in online Supplementary Material. On multivariate analysis, no significant correlation was found between the respondents' demographics and their attitude towards screening. The reasons for being keen or against cCMV screening are shown in Fig. 1. Notably, some participants commented that they still did not know what cCMV was at the end of the questionnaire.

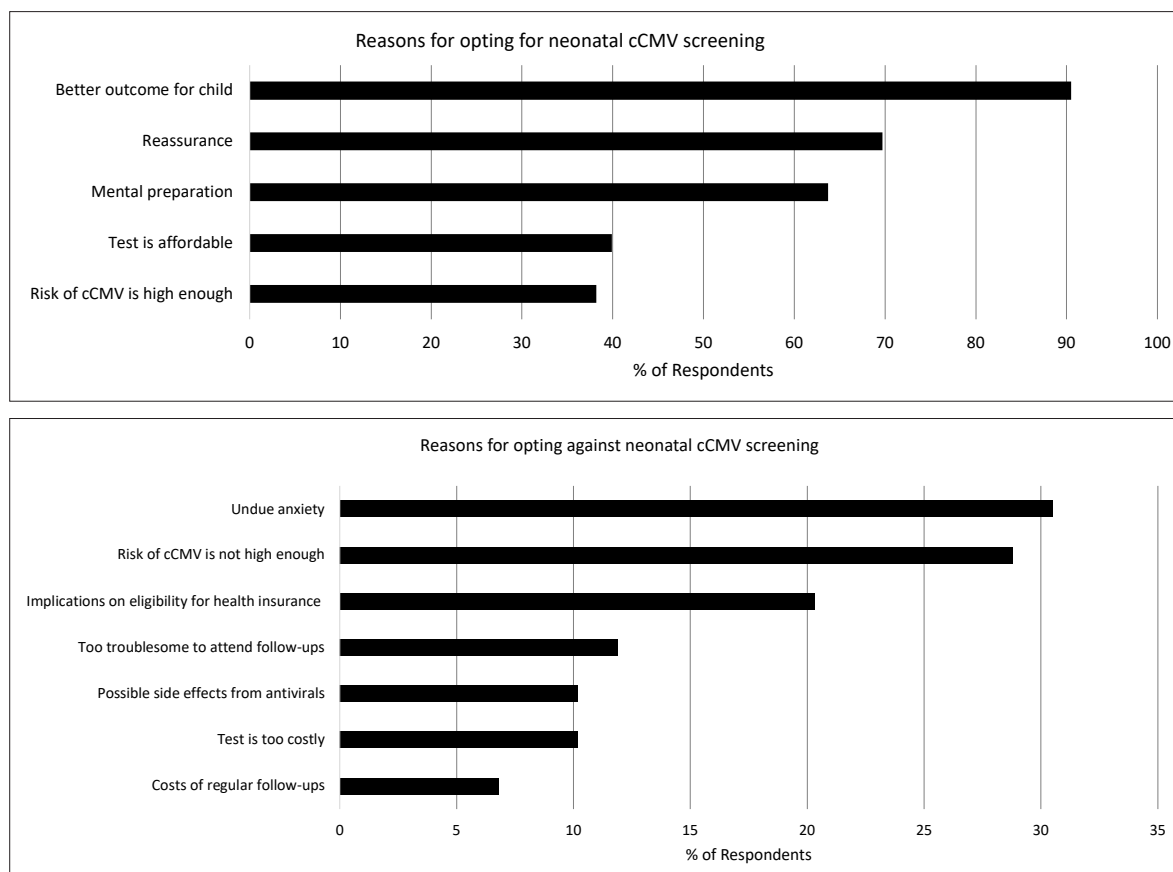


Fig. 1 Reasons for opting for and against neonatal congenital CMV (cCMV) screening.

From our study, it is apparent that awareness of CMV infection and its implications on infected newborns is low among the surveyed public. This is despite CMV being the most common congenital infection. As a priority, public education is of paramount importance. Primary prevention for seronegative mothers through infection control measures is simple and cost-effective.<sup>9</sup> Antenatal counselling of pregnant women attending outpatient clinics provides further opportunity to reduce mother-to-child CMV transmission. Simple hygiene precautions include not sharing food, drinks and utensils with young children; avoiding contact with saliva when kissing a child; and washing hands thoroughly after changing diapers, feeding a child or wiping a child's nose or saliva. These simple measures also help to prevent reinfection with a new CMV strain.

However, these measures have little impact on maternal CMV reactivation during pregnancy. Hence, in tandem with primary prevention, screening for cCMV should be considered to allow early detection and intervention. Having a known diagnosis also helps to minimise unnecessary investigations should the child develop symptoms in the future. Majority of respondents

in our study were keen to be given the option of newborn cCMV screening. Since few respondents were concerned about the cost of screening, it was unsurprising that we found no significant correlation between combined family income and attitude towards screening.

Trials are currently ongoing to assess the risks and benefits of antiviral treatment in asymptomatic, mildly symptomatic or isolated sensorineural hearing loss.<sup>9</sup> Assuming a modest benefit of antiviral treatment, studies have shown cCMV screening to be cost-effective.<sup>10</sup> Targeted screening for newborns of seropositive mothers is also a consideration. Screening using salivary CMV polymerase chain reaction (PCR) can be studied as part of a comprehensive newborn screening programme. Collecting saliva from newborns is easier than collecting urine. In addition, salivary PCR testing has been shown to be possibly more sensitive compared to urinary PCR.<sup>9</sup> Akin to genetic testing, adequate counselling on the implications of cCMV testing for the child and family is important prior to testing.

Until a vaccine becomes available, the importance of primary prevention through infection control measures and public education cannot be over-emphasised.

Secondary prevention with prenatal serologic screening for seroconversion coupled with immunoglobulin G avidity testing is another consideration. Ultimately, primary, secondary and tertiary prevention measures should be considered and implemented in tandem so that the outcome of newborns can be improved.

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