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Chapter 5

Awareness of congenital cytomegalovirus among doctors in the Netherlands

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Abstract

Background

Because of limited treatment options for congenital cytomegalovirus (CMV) infection, preventive strategies are important. Knowledge and awareness are essential for the success of preventive strategies.

Objectives

To investigate the knowledge of congenital CMV among doctors involved in mother and child care in the Netherlands.

Study design

A questionnaire on CMV infection was sent to doctors by snowball sampling. Knowledge concerning epidemiology, transmission, symptoms and signs of CMV infection in adults and children, and treatment options were evaluated.

Results

The questionnaire was completed by 246 doctors involved in mother and child care. The respondents estimated a prevalence of congenital CMV varying between 0.1 and 500 per 1000 live-born infants. The mean knowledge scores regarding transmission and postnatal symptoms increased with a more advanced career stage (i.e. older age). Gender and parenthood did not contribute to knowledge, but the field of expertise did. Respondents in the field of pediatrics had the highest mean score on postnatal symptoms and long-term effects. Respondents working in the field of gynecology and obstetrics were unaware of the precise transmission route of CMV. More than one-third of the respondents assumed that treatment was readily available for congenital CMV infection.

Conclusions

The knowledge of CMV infection among doctors in the Netherlands contained several gaps. Increasing knowledge and awareness is expected to enhance the prevention of transmission, to improve recognition, and to stimulate diagnostic investigations and follow-up programs.

Background

Congenital cytomegalovirus (CMV) infection is the most common congenital viral infection in newborns, with an estimated worldwide prevalence in live newborns of 0.64%.¹ Symptoms and signs are present at birth in 10–15% of these children, and another 15–20% will have sequelae that become apparent later in life.² We estimate that each year in the Netherlands approximately 800 children congenitally infected with CMV are born, of whom an estimated 160 will have long-term effects.³ The symptoms and signs of congenital CMV, such as intrauterine growth retardation (IUGR), elevated liver enzymes, convulsions, and long-term effects such as developmental delay and permanent childhood hearing impairment² have a great impact on the lives of children and their parents. Although several vaccines are being developed and tested, no vaccine has been licensed for use. Furthermore, in most countries no prenatal or neonatal screening program for congenital CMV infection exists, and only limited data exist on the effectiveness of prenatal or postnatal treatments.

While awaiting treatment options, the burden of disease can be decreased by preventive strategies that reduce the risk of transmission of CMV to the pregnant woman.^{4,5} A recent review of the implementation of educational hygiene interventions provides preliminary support for the positive effect of preventive strategies.⁶ The success of preventive strategies depends on the active involvement of the doctors involved in mother and child care.⁴ Awareness of the epidemiology, transmission, diagnosis and prevention of congenital CMV is essential for every doctor. Recent studies report on the knowledge of women of childbearing age, and obstetricians, concerning congenital CMV.^{7,8} One-fifth of the women of childbearing age had heard of congenital CMV, but only very few had specific knowledge about the clinical symptoms and signs, or the modes of transmission or prevention, even when these women were medical professionals themselves.

Half of the women who were aware of congenital CMV had heard about the virus from a doctor.⁷ A recent survey reported that most obstetricians do not include congenital CMV in their advisory consultation with their pregnant patients.⁸ Increased awareness of congenital CMV is important, not only to reduce the transmission rate, but also to improve the recognition of symptoms and signs in congenitally infected children.⁹ Such awareness could improve the subsequent diagnostic investigation and follow-up of these children, and allow treatment studies to be conducted.

Objectives

The objective of this study was to determine the knowledge of doctors involved in mother and child care in the Netherlands concerning congenital CMV.

Methods

Questionnaire development

A 12-item questionnaire on CMV, taking less than 4 min to complete, was developed. The questionnaire tested knowledge of the prevalence of congenital CMV; the symptoms and signs of CMV in healthy adults, newborns and children; the mode of transmission; and the treatment options. All but two questions regarding epidemiology and possible treatment were multiple choice. The possible answers were based on the literature, and included 20% false answers (i.e. non-symptoms). Multiple answers were accepted. Several demographic variables were asked for, including gender, age, parenthood and professional field. When a respondent had not heard of CMV at all, the questionnaire ended after recording the characteristics of the respondent. The questionnaire was pilot tested using a convenience sample, and ambiguous questions were rephrased. The questionnaire summary is given in Fig. 1.

What is the transmission route of cytomegalovirus?		
Air	Kissing	Breastfeeding
Sexual intercourse	Changing diapers	Don't know
Direct skin contact	Blood contact	
What is the most frequent presentation of CMV infection in immune competent adults?		
No symptoms	Not feeling well	Visual problems
Fever	Thrombosis	Don't know
Cardiac problems	Elevated liver enzymes	
What symptoms can be seen in newborns with congenital CMV infection?		
No symptoms	Microcephaly	Seizures
Petechiae	Growth retardation	Anal atresia
Elevated liver enzymes	Renal problems	Hearing loss
Congenital heart defect	Macrosomia	
What long-term effects can present in children with congenital CMV infection?		
Hearing loss	Visual problems	Obesity
Cognitive delay	Autism	Increased risk of malignancy
Cardiac problems	Seizures	Motor delay

Figure 1 Summary of CMV survey, including possible answers.

Sampling frame and questionnaire administration

The digital questionnaire, accompanied by a covering letter, was sent to the medical contacts of the researchers. Snowball sampling was used; all participants were asked to forward the link of the online questionnaire to medical colleagues.¹⁰ These contacts were interns, residents, hospital-based senior doctors, general practitioners and medical researchers. In addition to the digital questionnaire, a hard-copy version was completed by attendees at two local specialist meetings (Department of Pediatrics and Department of Otolaryngology). The questionnaire was anonymous, and the response period was closed after 2 months. One month after closure, an information brochure on congenital CMV was sent to all respondents who had indicated that they were interested. In this study the analysis was restricted to the replies of the doctors directly involved in mother and child care.

Data analysis

All statistical tests were carried out using SPSS version 16.0 (SPSS Inc., Chicago, IL, USA), with the significance level set at $P < 0.05$. Frequency responses to all questionnaire items were determined, and overall scores were calculated per questionnaire item. This overall score was based on the sum of the correctly stated true answers and the correctly not chosen false answers, assigning one point per correct answer. The maximum achievable score varied between 7 and 12 points, depending on the questionnaire item. Comparisons between different groups of respondents were made using χ^2 tests.

Results

The questionnaire was completed by 415 respondents, of whom 246 were involved in the care of mothers and children. The characteristics of the respondents and their mean scores on the questionnaire's topics are shown in Table 1. There were no significant gender differences in the mean scores. The mean knowledge scores regarding transmission and postnatal symptoms increased with a more advanced career stage (corresponding with an older age). Parenthood or plans to have children did not contribute significantly to knowledge of CMV infection. The field of expertise did contribute significantly to knowledge of CMV. Respondents in the field of infectious diseases had the highest mean knowledge score on transmission routes. The lowest (total) scores were achieved by general practitioners and otorhinolaryngologists. Respondents in the field of pediatrics had the highest mean score on postnatal

symptoms, as well as on knowledge of the long-term effects. The details and background variables of non-respondents could not be identified because of the sampling method used. The respondents estimated a prevalence of congenital CMV varying between 0.1 and 500 per 1000 live-born infants.

In Table 2, the number and proportion of stated true and false answers to CMV questionnaire items are shown. The relevant knowledge of respondents in pediatrics (postnatal symptoms and long-term effects) and respondents in gynecology and obstetrics (transmission route) is shown in detail. Fifty-six percent of the respondents were aware that CMV infection may not produce any symptoms in healthy adults. More than 50% of the respondents realized that microcephaly, growth restriction and hearing loss can be signs of congenital CMV in newborns, and the potential long-term effects were known by more than 65%. Half of the respondents thought air conduction was a true transmission route of congenital CMV. One-third of the pediatricians were aware that congenital CMV infection might not give rise to any symptoms at birth. Hearing loss and cognitive delay were accurately acknowledged as long-term effects of congenital CMV. Most of the respondents working in the field of gynecology and obstetrics were unaware of the precise transmission route of CMV. Of the respondents working in pediatrics, 55% were convinced that treatment options for congenital CMV infection were readily available, compared with 34.6% of the total respondents.

Table 1 Demographic variables of the respondents involved in mother and child care.

Characteristics	Number (%)	Mean transmission route score (max. possible = 7)	Mean adult symptom score (max. possible = 7)	Mean postnatal symptom score (max. possible = 12)	Mean long-term effect score (max. possible = 9)
Gender					
Male	65 (26.4)	3.2	4.9	7.4 ^a	5.2
Female	181 (73.6)	3.5	4.8	7.6	5.2
Career stage					
Resident	181 (73.6)	3.3 ^a	4.8	7.3 ^a	5.0
Senior doctor	65 (26.4)	3.8	4.9	8.3	5.5
Parenthood					
Having children or pregnant	205 (83.3)	3.8	4.9	7.9	5.3
No plans for children	41 (16.7)	3.4	4.8	7.5	5.3
Field of expertise					
Pediatrics	85 (34.5)	4.2 ^a	4.8 ^a	8.9 ^a	6.2 ^a
Gynecology and obstetrics	18 (7.3)	3.2	4.9	8.2	5.4
Oto-rhinolaryngology	13 (5.3)	3.2	4.5	6.9	5.3
General practice	121 (49.2)	2.8	4.9	8.2	5.4
Infectious diseases (incl. medical microbiology)	9 (3.7)	5.1	5.1	8.2	5.7
Total	246	3.4	4.8	7.5	5.2

^aP < 0.05.

Table 2 The number and percentage of stated "yes" responses per multiple-choice item on the CMV questionnaire for all respondents and for respondents in pediatrics and obstetrics and gynecology in more detail.

Knowledge concerning	Total number of respondents (n = 246) (%)	Number of pediatricians (n = 85) (%)	Number of obstetricians and gynecologists (n = 18) (%)
Transmission route			
True answers			
Kissing	129 (52.4)	40 (47.1)	7 (38.9)
Changing diapers	56 (22.8)	34 (40)	4 (22.2)
Breast milk	85 (34.6)	42 (49.4)	8 (44.4)
Blood contact	141 (57.3)	69 (81.2)	11 (61.1)
Sexual intercourse	98 (39.8)	43 (50.6)	8 (44.4)
False answers			
Air conduction	126 (51.2)	31 (36.5)	9 (50.0)
Direct skin contact	38 (15.5)	9 (10.6)	6 (33.3)
Symptoms in immune competent adults			
True answers			
No symptoms	137 (55.7)	60 (70.6)	10 (55.6)
Not feeling well	159 (64.6)	48 (56.5)	14 (77.8)
Fever	88 (35.8)	25 (29.4)	8 (44.4)
Elevated liver enzymes	72 (29.3)	21 (24.7)	5 (27.8)
False answers			
Cardiac problems	0 (0)	0 (0)	0 (0)
Thrombosis	0 (0)	0 (0)	0 (0)
Visual problems	5 (2.0)	1 (1.2)	2 (11.1)
Postnatal symptoms			
True answers			
No symptoms	50 (20.3)	27 (31.8)	3 (16.7)
Petechiae	71 (28.9)	45 (52.9)	5 (27.8)
Elevated liver enzymes	109 (44.3)	57 (67.1)	5 (27.8)
Microcephaly	138 (56.1)	73 (85.0)	12 (66.7)
IUGR	146 (59.3)	61 (71.8)	16 (88.9)
Hearing loss	138 (56.1)	67 (78.8)	12 (66.7)
Seizures	68 (27.8)	40 (47.1)	6 (33.3)
False answers			
Heart defect	53 (21.6)	20 (23.5)	1 (5.6)
Macrosomia	2 (0.8)	0 (0)	0 (0)
Renal problems	29 (11.8)	13 (15.3)	1 (5.6)
Anal atresia	1 (0.4)	0 (0)	0 (0)

Long-term effects

True answers			
Hearing loss	161 (65.5)	78 (91.8)	13 (72.2)
Cognitive delay	171 (69.5)	77 (90.6)	15 (83.3)
Motor delay	89 (36.2)	42 (49.4)	6 (33.3)
Seizures	49 (19.9)	32 (37.6)	0 (0)
Autism	10 (4.1)	6 (7.1)	0 (0)
Visual problems	99 (40.2)	50 (58.8)	11 (61.1)
False answers			
Cardiac problems	39 (15.9)	14 (16.5)	1 (5.6)
Obesity	1 (0.4)	0 (0)	0 (0)
Increased risk for malignancy	4 (1.6)	2 (2.4)	0 (0)
There is treatment available	85 (34.6)	47 (55.3)	5 (27.8)

Note that multiple answers were accepted so the percentage adds up to more than 100%.

Discussion and conclusion

We investigated the knowledge of congenital CMV infection among doctors in the Netherlands involved in mother and child care. Several interesting findings were shown. First, doctors seemed to miscalculate the chance of encountering a child with congenital CMV infection in medical practice. There seemed to be a risk of underdiagnosis, since the prevalence of congenital CMV, internationally estimated to be 0.64%, was sometimes overestimated, but more frequently underestimated by respondents in this study. Secondly, preventive strategies are assumed to be effective only when doctors are sufficiently well informed to advise their patients properly. The data in this study show that most of the doctors were aware that most healthy adults and pregnant women do not experience any symptoms of a CMV infection. Worryingly, however, only one-fifth of the respondents, including those working with pregnant patients, were aware that kissing, and changing diapers, are risk factors for the transmission of CMV. Thirdly, including congenital CMV infection in the differential diagnosis in symptomatic newborns is crucially important. Since only half of the total respondents in this study and two-thirds of those working in pediatrics were aware that microcephaly, IUGR and hearing loss could be symptoms of congenital CMV, it seems possible that these children may be left undiagnosed, with possibilities for treatment and follow-up not explored. It is worrying that only 20% of all respondents and 32% of respondents in pediatrics realized that congenital CMV frequently does not give rise to any symptoms and signs at birth, and that 14% of these asymptomatic newborns will develop long-term sequelae.² Finally, we were surprised that 55% of the

respondents in the field of pediatrics thought that the antiviral therapy of newborns with congenital CMV infections is common practice in the Netherlands. Even though antiviral therapy has been shown to prevent hearing deterioration in newborns with symptomatic CMV infections, this practice is not yet widespread here.¹¹

This study has several shortcomings: the sampling frame and questionnaire administration might have introduced bias, since the invitation started among the medical contacts of the researchers. These contacts might have had an advantage in knowing more about congenital CMV. Additionally, completing the questionnaire might have been subject to response bias, since respondents who felt unsure about their knowledge of CMV could refuse to respond to the questionnaire. This bias, however, might imply that the true knowledge concerning congenital CMV infection is even poorer than reported.

Medical information is available from various sources: Internet, TV, radio, newspapers and magazines. However, information is generally not sought if the public is not aware of a health risk or health problem. It is the responsibility of a doctor to be aware of the risks to a population in special situations, and supply information to reduce the health risk. When the doctor lacks awareness, this information is not available to the population or the individual patient. In the case of CMV it is especially important that doctors involved in the care of women who are or who may become pregnant are able to advise on the risk of congenital CMV and how this risk may be reduced. To date, information on congenital CMV is not regularly included in preconception and antenatal consultations. Fig. 2 gives a brief overview of what doctors should know about congenital CMV infection, for those working in pediatrics or obstetrics and gynecology.

In summary, this study focused on one of the essential aspects of successful preventive strategies for congenital CMV infections: the knowledge of doctors involved in mother and child care. Consistent with earlier findings, we show that most doctors concerned with mother and child care in the Netherlands do not possess optimal knowledge on CMV. The results of this study can be used for discussions on awareness and relevant knowledge for each specific medical field, individualized education for doctors, and for the development of preventive strategies. Awareness and knowledge will subsequently improve the recognition of early and late symptoms and signs, improve diagnostic and follow-up programs, and might even promote the development of evidence-based treatment in the near future.

Pediatricians	Obstetricians and gynecologists
<p>Presentation of congenital infection in newborns</p> <ul style="list-style-type: none"> • Asymptomatic • Growth retardation and/or microcephaly • Hearing loss • Thrombocytopenia • Elevated liver enzymes 	<p>Presentation of CMV infection in adults</p> <ul style="list-style-type: none"> • Asymptomatic • Fever • Elevated liver enzymes
<p>Late effects of congenital infection</p> <ul style="list-style-type: none"> • Hearing loss • Developmental delay 	<p>Transmission route</p> <ul style="list-style-type: none"> • Body fluids • Blood contact
<p>Estimated prevalence in newborns</p> <p>0.64% worldwide</p>	<p>Preventive strategies</p> <ul style="list-style-type: none"> • Wash hands after changing diapers • Avoid kissing young children on the mouth • Don't share food, drink or cutlery with young children

Figure 2 What doctors should know about congenital CMV infection.

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