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Changing patterns of cytomegalovirus seroprevalence among pregnant women in Norway between 1995 and 2009 examined in the Norwegian Mother and Child Cohort Study and two cohorts from Sør-Trøndelag County: a cross-sectional study

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ABSTRACT

Objectives: To examine cytomegalovirus (CMV) seroprevalence and associated risk factors for CMV seropositivity in pregnant Norwegian women.

Design: Cross-sectional study.

Setting: The Norwegian Mother and Child Cohort Study (MoBa) in addition to two random samples of pregnant women from Sør-Trøndelag County in Norway.

Participants: Study group 1 were 1000 pregnant women, randomly selected among 46 127 pregnancies in the MoBa (1999–2006) at 17/18 week of gestation. Non-ethnic Norwegian women were excluded. Study groups 2 (n=1013 from 1995) and 3 (n=979 from 2009) were pregnant women at 12 weeks of gestation from Sør-Trøndelag County.

Outcome measures: CMV seropositivity in blood samples from pregnant Norwegian women.

Results: CMV-IgG antibodies were detected in 59.9% and CMV-IgM antibodies in 1.3% of pregnant Norwegian women in study group 1. Women from North Norway demonstrated a higher CMV-IgG seroprevalence (72.1%) than women from South Norway (58.5%) (OR 1.83, 95% CI 1.17 to 2.88). The CMV-IgG seroprevalence was higher among women with low education (70.5%) compared to women with higher education (OR 2.20, 95% CI 1.24 to 3.90). Between 1995 and 2009 the CMV-IgG seroprevalence increased from 63.1% to 71.4% in pregnant women from Sør-Trøndelag County (study groups 2 and 3; p<0.001). The highest CMV-IgG seroprevalence (79.0%) was observed among the youngest pregnant women (<25 years) from Sør-Trøndelag County in 2009 (study group 3).

Conclusions: The CMV-IgG seroprevalence of pregnant Norwegian women varies with geographic location and educational level. Additionally, the CMV-IgG seroprevalence appears to have increased over the last years, particularly among young pregnant women.

ARTICLE SUMMARY

Strengths and limitations of this study

- The national population-based design and the opportunity to assess regional differences in cytomegalovirus (CMV)-IgG seroprevalence.
- The Norwegian Mother and Child Cohort Study may be disposed to some self-selection. Such skewed selection of women in the Norwegian Mother and Child Cohort Study may potentially lead to an underestimation of CMV-IgG seroprevalence.
- Two comparable study groups from the same population with 14 years interval made it possible to give a good estimate of time trends in CMV seroprevalence.

INTRODUCTION

Pregnancy is associated with a functional immunosuppression and, thus, may increase the risk of acquiring infections.[1] Cytomegalovirus (CMV) infection is a common viral infection in pregnancy[2] and may have severe consequences for the developing fetus.[3] About 0.15–2.0% of live-born neonates are infected with CMV[4] and this may result in symptoms ranging from sensorineural hearing loss to multiorgan failure.[3] There is currently no effective treatment for congenital CMV infection.[5]

The CMV virus persists in the host for life and may become reactivated during pregnancy.[6] Recurrent CMV infection may either include reactivation of a latent virus or a reinfection with a different CMV strain.[6] About 1–4% of CMV-IgG seronegative pregnant women will acquire a CMV infection for

the first time during pregnancy[7 8] and about 30% of these transmit the virus to the fetus, resulting in congenital infection.[2] In contrast, the transmission rate is around 1% during recurrent CMV infections.[2] Recurrent CMV infections are common in pregnancy and constitute the majority of congenital infections in populations with high CMV-IgG seroprevalence.[9 10]

The CMV-IgG seroprevalence among women in reproductive age ranges from 30% to 100% in different populations.[9 11–23] Elements influencing CMV-IgG variability are geography, socioeconomic status (SES) and the woman's age and parity.[12 13 15 21 22] The highest CMV-IgG seroprevalence in pregnant women of 70–100% has been observed in Africa, Asia and South America.[9 15–17] Pregnant women in industrialised countries in Western Europe and North America have demonstrated lower CMV-IgG seroprevalence levels of about 30–50%.[11–15 21–23] Factors associated with CMV-IgG seropositivity in developed countries are non-White race and lower SES.[21 22] The high CMV-IgG seroprevalence in developing countries is probably due to lower SES and poor hygienic conditions. Countries like Spain, Japan and Germany has experienced a decrease in CMV-IgG seroprevalence.[17 18 23 24] This could be explained as an improvement of SES in these countries. CMV is known to be transmitted through breast milk and infected infants shed virus in the urine years after inoculation.[25–27] Thus, increased use of breastfeeding and day-care centre are suggested reasons for higher CMV-IgG seroprevalence in some developed countries, such as Sweden.[28]

Since socioeconomic factors may influence acquisition patterns of viruses, updated studies are needed to monitor the level of immunity in a population. Norway is a highly developed country with a population of about 5 million people and 60 000 yearly deliveries. Two previous studies on CMV seroprevalence in pregnant Norwegian women demonstrated CMV-IgG prevalences of 69% (in 1992–1994)[19] and 62.3% (in 2001),[20] respectively. However, both studies only addressed the overall CMV-IgG seroprevalence[19 20] and the study from 2001 was rather small (n=69).[20] Thus, the aim of the present study was to (1) examine the seroprevalence of CMV-IgG and CMV-IgM antibodies in pregnant Norwegian women and (2) investigate the influence of geography, age, parity, education and income and (3) assess changes in CMV seroprevalence over time.

METHODS

Study design and study population

This is a cross-sectional study including three study populations of pregnant Norwegian women. In study group 1, The Norwegian Mother and Child Cohort Study (MoBa) was included to assess CMV seroprevalence nationwide and to investigate the influence of selected risk factors. In study groups 2 and 3 two populations from Sør-Trøndelag County collected at 14 years interval were included to allow investigation of time trends.

Study group 1

The MoBa is a prospective population-based pregnancy cohort study conducted by the Norwegian Institute of Public Health.[29 30] Participants were recruited from all over Norway in 1999–2008 and 38.5% of invited women consented to participate. The cohort now includes 108 000 children, 90 700 mothers and 71 500 fathers. Blood samples were obtained from both parents during pregnancy and from mothers and children (umbilical cord) at birth. Follow-up is conducted by questionnaires at regular intervals and by linkage to national health registries. Several substudies are conducting additional collections of data and biological materials.

For this study, a group of 1000 women were randomly selected from the total of 46 127 pregnancies included in the MoBa in 1999–2006. One of these women had participated with two pregnancies and her second pregnancy was excluded. Forty-two women stated that their first language was not Norwegian and were excluded from the overall analyses because of known ethnic variances in CMV seroprevalence.[13 15] Therefore, study group 1 comprised a total number of 957 women and plasma samples collected from women at the 17/18 gestational week were used to examine levels of CMV-IgG and CMV-IgM antibodies.

Study group 1 included all Norwegian counties and was further divided into two large geographical regions; North Norway (including Sør-Trøndelag County and all counties further north) and South Norway (including all counties south of Sør-Trøndelag County). The women were divided into four age-defined groups; <25, 25–30, 31–35 and >35 years of age. Parity was divided into three groups; para 0, para 1 or para 2+. Information about education and income level was obtained from the MoBa questionnaires. Education was divided into four different categories; Elementary School, Secondary School, University Education <4 years or University Education >4 years. Income was classified into three groups of annual family income; low (< €19 809/year for at least one parent), middle (€19 809–€52 826/year for each parent) and high (>€52 826/year for at least one parent).

The MoBa population has been used for several substudies and linked to national health registries. The Medical Birth Registry of Norway (MBRN) includes information on all pregnant and delivering Norwegian women since 1968.[31] Comparison of MoBa and MBRN registered pregnancies has shown more healthy pregnancies among MoBa women than for the general population of pregnant Norwegian women.[32] Thus, to compare the status of study group 1 to all pregnant Norwegian women, MBRN registered Norwegian women delivering in 1996–2006 (n=453 395) was used for comparison.

Study groups 2 and 3

To investigate changes in CMV seroprevalence over time, serum samples collected in 1995 (study group 2) and 2009 (study group 3) from pregnant women in

Sør-Trøndelag County, a county in middle Norway, were tested and compared. Sør-Trøndelag County has 290 000 inhabitants, with nearly 60% of the population living in the city of Trondheim. In 2009, 3335 live born children were born in Sør-Trøndelag County.[31] Antenatal care includes blood samples collected at first health visit between 8 and 12 weeks of pregnancy and blood samples from all pregnant women in the county are sent to the Department of Medical Microbiology at St. Olavs Hospital, Trondheim University Hospital, for rubella antibody analysis. Study group 2 include sera from pregnant women (n=1013) sent for rubella screening in 1995 and study group 3 include sera from pregnant women (n=979) sent for rubella screening in 2009. Thus, study groups 2 and 3 were randomly selected pregnant women from the same county with sera collected at similar conditions and analysed in the same laboratory for the presence of CMV-IgG and CMV-IgM antibodies. In study group 3 information was available on female age, and ages were divided into four age groups; <25, 25–30, 31–35 and >35 years of age.

CMV antibody testing

Plasma samples from study group 1 were stored at −80°C and serum samples from study groups 2 and 3 were stored at −20°C before testing. Antibody levels of CMV-IgG and CMV-IgM in all samples were determined by an ELISA (Medac, Hamburg, Germany). The sensitivity and specificity for the Medac CMV-IgG kit have been estimated to 95.5–100% and 99.5%, respectively.[33] The Medac CMV-IgM kit has shown a very good specificity in independent evaluations.[34]

Seropositivity was defined according to the guidelines given by the manufacturer. Sera yielding equivocal values (for IgG; study group 1 (n=34) and study groups 2 and 3 (n=50) and for IgM; study group 1 (n=7) and study groups 2 and 3 (n=10)), were excluded from further analysis. Identical tests from the same manufacturer were used for analysing samples from all three cohorts studied.

Statistical analysis

The primary outcome variable in this study was CMV seropositivity, defined as the presence of CMV-IgG or CMV-IgM antibodies in serum or plasma. CMV seroprevalence is defined as the prevalence of CMV seropositivity in a population.

All seroprevalence data were assessed as proportions (per cent) with CIs of 95%. Univariate differences in the proportions between groups were tested by χ^2 test and logistic regression test was used to calculate crude and adjusted ORs of CMV seroprevalence by selected predictors in bivariate and trivariate regression models. The predictors were place of residence, age group, parity, educational level, maternal income and family income. Maternal age and education are both factors known to influence CMV seroprevalence and were adjusted for by logistic regression.

Two-sample t test was used to compare continuous data between CMV seronegative and seropositive mothers. Women with missing data were excluded from the analysis. The level of statistical significance was set to $p<0.05$. All statistical analyses were performed using the Predictive Analytics Software statistics V.18 (Chicago, Illinois, USA).

RESULTS

Characteristics of the pregnant Norwegian women in study group 1

Most women (88.8%) in study group 1 selected from the MoBa reside in South Norway. Women of age groups 25–30 and 31–35 years were dominating in study group 1 (44.0% and 34.1%, respectively) and most women were para 0 (42.6%) or para 1 (37.5%; table 1). The level of education was fairly high (20.1% with >4 years and 40.6% with <4 years of higher education) and most women (48.7%) were in the middle family income

Table 1 Characteristics of study group 1 selected from the Norwegian Mother and Child Cohort Study, 1999–2006

	Study group 1 (n=957)	Proportions (95% CI)
Place of residence*		
North Norway	107	11.2 (9.3 to 13.4)
South Norway	848	88.8 (88.6 to 90.7)
Maternal age in years*		
Overall mean (SD) (%)		29.8 (4 to 5)
<25	118	12.4 (10.4 to 14.7)
25–30	420	44.0 (40.6 to 47.2)
31–35	326	34.1 (31.1 to 38.2)
>35	91	9.5 (7.6 to 11.4)
Parity (%)*		
0	407	42.6 (39.6 to 45.8)
1	358	37.5 (34.6 to 40.5)
2+	190	19.9 (17.4 to 22.2)
Educational level†		
High school (>4 years)	177	20.1 (17.5 to 22.9)
High school (≤4 years)	358	40.6 (37.4 to 44.0)
Secondary school	268	30.4 (27.4 to 33.6)
Elementary school	78	8.9 (7.1 to 10.9)
Income‡		
High	257	28.1 (25.5 to 31.2)
Middle	445	48.7 (45.5 to 52.0)
Low	211	23.1 (20.4 to 25.6)

*Missing values N=2.
†The education achieved by the women is given at separated levels, where high education is referred to as University Education, missing values on education N=77.
‡Income was classified into three groups of annual income; low (<€19 809/year), middle (€19 809–€52 826/year) and high (>€52 826/year), missing values for income N=44.

category, while 28.1% of the women were in the high family income category (table 1). Smoking prevalence among the pregnant women in study group 1 was 12.7% (data not shown).

The characteristics of study group 1 corresponded to the MBRN registered general population of pregnant Norwegian women regarding geography (81.7% gave birth in South Norway and 18.3% in North Norway), age and parity.[31] However, study group 1 included fewer smokers than the general population of pregnant women (12.7% vs 15.7%). Additionally, fewer premature babies (4.1% vs 7.2%), higher birth weight (3641 vs 3526 g), higher gestational age (39.5 vs 39.3 weeks) and fewer children with low birth weight (1.8% vs 5.2%) were observed in study group 1 selected from MoBa than in the general population of pregnant Norwegian women delivering between 1996 and 2006.

CMV antibodies among pregnant Norwegian women in study group 1

In total, the seropositivity rate of CMV-IgM antibodies, indicating a recent CMV infection, was 1.3% (95% CI 0.6% to 2.2%) (n=947), whereas the CMV-IgG seroprevalence was 59.9% (95% CI 56.7% to 63.1%; n=923) in study group 1. The influences of geography, age, parity, education and income on CMV-IgG seroprevalence among the pregnant Norwegian women of study group 1 are given in table 2. Women from North Norway demonstrated a higher CMV-IgG seroprevalence (72.1%) than those from South Norway (58.5%; p<0.01; table 2).

No significant difference in CMV-IgG seroprevalence was observed with relation to woman's age and parity, although a tendency towards higher CMV-IgG seroprevalence (65.5%) was observed among the youngest women (<25 years of age) compared with the elder groups (table 2).

Women with the lowest educational level demonstrated a higher CMV-IgG seroprevalence (70.5%) compared with the highest education level (52.0%; p<0.01; table 2). Different levels of education between women from North Norway and South Norway were observed (21.3% women reported >4 years of higher education in South Norway compared to 10.4% women in North Norway). The CMV-IgG seropositive data in North Norway and South Norway were adjusted for education and the OR for being CMV-IgG seropositive in North

Table 2 Cytomegalovirus (CMV)-IgG seropositivity according to selected risk factors in pregnant Norwegian women in study group 1 from the Norwegian Mother and Child Cohort Study, 1999–2006

	Study group 1 (n=923)†	CMV-IgG seropositive n (%)	Crude OR‡ (95% CI)	Adjusted OR§ (95% CI)	Adjusted OR¶ (95% CI)
Place of residence††					
South Norway	817	478 (58.5)	1.00	1.00	1.00
North Norway	104	75 (72.1)	1.83 (1.17 to 2.88)*	1.81 (1.15 to 2.84)*	1.56 (0.97 to 2.49)
Age group in years††					
<25	116	76 (65.5)	1.00		1.00
25–30	404	231 (57.2)	0.70 (0.46 to 1.08)		0.78 (0.48 to 1.13)
31–35	314	193 (61.5)	0.84 (0.54 to 1.31)		0.98 (0.58 to 1.64)
>35	87	53 (60.9)	0.82 (0.46 to 1.46)		1.04 (0.56 to 1.96)
Parity††					
0	391	230 (58.8)	1.00	1.00	1.00
1	343	202 (58.9)	1.00 (0.75 to 1.35)	1.02 (0.75 to 1.38)	0.94 (0.69 to 1.28)
>2	187	121 (64.7)	1.28 (0.89 to 1.84)	1.34 (0.91 to 1.96)	1.21 (0.83 to 1.77)
Education‡‡					
High school (>4 years)	171	89 (52.0)	1.00	1.00	
High school (≤4 years)	343	212 (61.8)	1.49 (1.03 to 2.16)**	1.56 (1.07 to 2.27)**	
Secondary school	256	152 (59.4)	1.35 (0.91 to 1.99)	1.38 (0.91 to 2.09)	
Elementary school	78	55 (70.5)	2.20 (1.24 to 3.90)*	2.21 (1.21 to 4.04)*	
Income§§					
High	247	133 (53.8)	1.00	1.00	1.00
Middle	427	260 (60.9)	1.33 (0.97 to 1.83)	1.40 (1.01 to 1.94)**	1.31 (0.95 to 1.82)
Low	205	129 (62.9)	1.46 (1.00 to 2.12)	1.51 (1.00 to 2.28)**	1.32 (0.87 to 2.02)

*p<0.01.
**p<0.05.
†Equivocal results N=34 were excluded.
‡OR for CMV seropositivity was calculated by logistic regression in successive bivariate (crude OR) and trivariate (adjusted OR) models.
§Adjusted for age N=921.
¶Adjusted for education N=846.
††Missing values N=2.
‡‡The education achieved by the women is given at separated levels, where high education is referred to as University education, missing values on education N=77.
‡‡Income was classified into three groups of annual income; low (<€19 809/year), middle (€19 809–€52 826/year) and high (>€52 826/year), missing values for income N=44.

Table 3 Cytomegalovirus (CMV)-IgG seropositivity according to maternal age in study group 3, pregnant women in Sør-Trøndelag County, 2009

	Study group 3 (n=929)†	CMV-IgG seropositive n (%)	Crude OR (95% CI)
Age group in years			
<25	176	139 (79.0)	1.00
5–30	394	268 (68.0)	0.57 (0.37 to 0.86)*
31–35	251	182 (72.5)	0.70 (0.46 to 1.11)
>35	108	74 (68.5)	0.60 (0.34 to 1.00)**

*p<0.01.
**p<0.05.
†Equivocal results N=50 were excluded.

Norway compared to South Norway was reduced to 1.56 (95% CI 0.97 to 2.49). Even though the adjusted OR was not significant, geography still remained a strong predictive factor for CMV-IgG seropositivity. A negative and statistically significant linear trend was observed between CMV-IgG seroprevalence and family income (linear χ^2=4.03, p<0.05). Low income was associated with close to 50% higher CMV-IgG seropositivity (compared to the high family income).

CMV antibodies among pregnant women from Sør-Trøndelag County in study groups 2 and 3

Comparing the pregnant women from Sør-Trøndelag County collected in 1995 (study group 2) and 2009 (study group 3), revealed interesting differences in CMV-IgG seroprevalence. The CMV-IgG seroprevalence in 1995 was 63.1% (95% CI 60.0% to 66.1%), while in 2009, the CMV-IgG seroprevalence showed a marked increase to 71.4% (95% CI 68.3% to 74.3%; p<0.01). Similar changes were not observed for CMV-IgM (1995: 1.3%, 95% CI 0.69% to 2.18% and 2009: 1.7%, 95% CI 0.95% to 2.67%).

The age of the study group 2 women was not available, but the mean age of the 3544 women delivering in Sør-Trøndelag in 1995 was 28.0 (SD=4.9 years).[31] The mean age of the study group 3 women from 2009 was 29.1 years (SD=5.2 years) and the mean age for all the 3780 women giving birth in Sør-Trøndelag in 2009 was 29.6 (SD=5.2).[31] The CMV-IgG seroprevalence related to the women's age groups in study group 3 is presented in table 3. Generally, CMV-IgG seropositive (26.9 years, SD=4.7 years) and seronegative (29.1 years, SD=5.2 years) groups demonstrated no significant age difference (p=0.14). However, the youngest women (<25 years of age) in study group 3 demonstrated the highest CMV-IgG seropositivity (79%), as compared to women above 25 years of age (69.5% seropositivity; p<0.01).

DISCUSSION

This study shows an overall seroprevalence of 59.9% for CMV-IgG and 1.3% for CMV-IgM among pregnant Norwegian women (study group 1). The strongest risk factors for CMV-IgG seropositivity were place of residence (highest CMV-IgG seropositivity in North Norway (72.1%)) and low education (70.5%). More women with higher education were living in South Norway than North Norway and this could explain some of the geographical differences observed. The comparison of two random samples of pregnant women in Sør-Trøndelag County (study groups 2 and 3) suggested a CMV-IgG seroprevalence increase over time, from 63.1% in 1995 to 71.4% in 2009. Interestingly, the highest CMV-IgG seropositivity rate (79%) was detected in young women (<25 years).

The strength of this study is the national population-based design of study group 1 and the opportunity to assess regional differences in CMV-IgG seroprevalence. A limitation to this study is that the MoBa may be disposed to some self-selection. Nilsen *et al*[32] reported that the women in the MoBa had experienced somewhat healthier pregnancies as compared with the general pregnant population in Norway, and this is also reflected in our study group 1 from the MoBa. However, birth weight and prematurity, which were different between MoBa and MBRN in this material, have not been associated with CMV-IgG seropositivity and should therefore not have influenced the results.[19 35] A higher level of education was also observed in our study group from the MoBa than generally in Norwegian women of the same age groups.[36] Since high SES is negatively correlated with CMV-IgG seropositivity,[13 15 21 22] such skewed selection of women in the MoBa may potentially lead to an underestimation of CMV-IgG seroprevalence. However, when women from Sør-Trøndelag County included in the MoBa (n=19; study group 1) were compared with the Sør-Trøndelag random sample from 2009 (study group 3), fairly similar CMV-IgG seroprevalences were observed (73.7% in the MoBa and 71.4% in the Sør-Trøndelag random sample). It is therefore likely that the estimates from the MoBa population represent the true CMV-IgG seroprevalence in the pregnant Norwegian population. Missing data among some women in study group 1 could potentially bias the results of the multivariate logistic regression analyses. These women, however, have a higher CMV-IgG seroprevalence and are most likely lesser educated, hence the associations presented are underestimates rather than overestimates.

Although the Sør-Trøndelag groups (study groups 2 and 3) represent two unselected groups of pregnant women, we cannot exclude the possibility that the increasing immigration of non-ethnic Norwegians (from 2.5% in 1996 to 5.5% in 2009)[37] could explain some of the increase in CMV-IgG seroprevalence. However, a 3% increase in non-ethnic Norwegians would lead to only about a 1% increase in CMV-IgG seroprevalence, leaving a change in the ethnic composition an unlikely explanation for the increasing trend in CMV-IgG seroprevalence over time. The youngest women <25 years had the

highest CMV-IgG seroprevalence and the increasing trend in CMV-IgG seroprevalence could possibly be due to an increased proportion of young pregnant women in the population. However, in line with an increasing mean age of delivering women in Norway (1995: 28.3 years, 2009: 29.7 years), the proportion of delivering women <25 years of age in Sør-Trøndelag County was 24.6% in 1995 and only 16.7% in 2009.[31]

Sør-Trøndelag County, located in the middle of Norway, represents a typical Norwegian region. This study showed a statistically significant increase in CMV-IgG seroprevalence among pregnant women from 1995 to 2009 (study groups 2 and 3). Additionally, the group from Sør-Trøndelag County in 2009 demonstrated a particularly high CMV-IgG seroprevalence among the youngest pregnant women. This is in contrast to other studies, reporting an increased CMV-IgG seroprevalence with increased age.[12 15 18] Our findings suggest that more Norwegian women are CMV infected as children and teenagers now than before and indicate that the CMV-IgG seroprevalence among pregnant Norwegian women may be further increasing. This hypothesis is supported by findings in the MoBa, where the youngest pregnant women also demonstrated the highest CMV-IgG seroprevalence, suggesting that the increase in CMV-IgG seroprevalence may be occurring at a national level.

Despite high socioeconomic conditions in the Scandinavian countries, the CMV-IgG seroprevalence seem to be relatively high. Including our estimates, CMV-IgG seroprevalence in Norway and Sweden ranges between 60% and 73%,[19 20 38] whereas in other highly developed countries such as the Netherlands, Ireland, Canada and France, the CMV-IgG seroprevalence numbers are reported as low as 30–50% among pregnant Caucasian women.[11–15] As a country becomes more developed, hygiene and socioeconomic conditions improves and thus the CMV-IgG seroprevalence is expected to decrease as reported in Spain, Japan and Germany.[17 18 23 24] The surprisingly high CMV-IgG seroprevalence levels in Norway may probably be ascribed to high incidence of breastfeeding and children attending group day-care facilities. Breast milk from CMV-IgG seropositive women contains detectable CMV-DNA and infectious virus[39] which can be transmitted to the newborn baby.[26] Group day-care is also well known to increase the frequency of CMV infections in childhood.[27 40] Both customs have increased in Norway since the 1970s.[41–44] Today, about 98% of Norwegian children are breastfed during the first week of life, while 89.7% of all children attend day-care centre.[43 45] Accordingly, these changes may have influenced the increase in CMV-IgG seroprevalence observed among young pregnant women of Sør-Trøndelag County in this study. A relation between high breastfeeding rates and the use of day-care centre in developed countries has previously been suggested as a reason for high CMV-IgG seroprevalence rates,[28] but updated Norwegian studies supporting this have been missing. This study provides contemporary data on an increase in CMV-IgG seroprevalence among pregnant Norwegian women supporting this hypothesis. There are also regional differences in breastfeeding and the use of day-care centre in Norway, but these are too small to explain the differences in CMV-IgG seroprevalence.[46]

This study demonstrates that CMV-IgG seroprevalence in pregnant Norwegian women is relatively high, especially for a developed country. The frequency is highest in the northern region and associated with fewer years of education. The observed CMV-IgG seroprevalence increase observed during the last 14 years, especially among the youngest women, may be due to increased breastfeeding rates of long duration and regular use of day care center in the Norwegian society.

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Contributors MLO analysed the data and wrote the manuscript. KMS contributed to the data analysis and writing of the manuscript. SAN participated in the data interpretation and was responsible for the study design and serological testing. SF supervised the statistical analyses, the data interpretation and revised the manuscript. ACI was responsible for the research hypothesis, the study design and revision of the manuscript. RA contributed to the idea and to the writing of the manuscript. All authors have approved the final version of the manuscript.

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Competing interests None.

Ethics approval The current study is based on V.4 of the quality-assured data files of the Norwegian Mother and Child Cohort Study (MoBa) participants recruited from 1999 to 2006. Informed consent was obtained from each MoBa participant upon recruitment. The study was approved by The Regional Committee for Medical Research Ethics in South Eastern Norway 27.02.2006 (S-06072), and obtained a license from the Data Inspectorate in Norway 25.01.2006 (2005/167–2). The samples from Sør-Trøndelag in study group 2 and 3 are from anonymous quality assessment and ethical approval for research purpose is not requested according to the Norwegian Health Research Act.

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