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MAJOR ARTICLE

Cytomegalovirus Seroprevalence Among Children and Adolescents in Germany: Data From the German Health Interview and Examination Survey for Children and Adolescents (KiGGS), 2003–2006

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Background. Congenital cytomegalovirus (CMV) infection can cause severe birth defects. The majority of children with congenital CMV are born to CMV-seropositive women; however, transmission from mother to fetus and resulting defects are more likely to occur when mothers experience seroconversion during pregnancy. The objective of this study was to provide a population-based estimate of CMV seropositivity and to identify factors that correlate with the detection of CMV-immunoglobulin (Ig)G antibodies.

Methods. Cytomegalovirus-specific IgG antibodies were determined by enzyme-linked immunosorbent assay in 13 876 serum samples from children and adolescents (aged 1–17 years). Cytomegalovirus seroprevalence was correlated with children's age, gender, migration background, country of origin, place of birth, socioeconomic status, breast feeding, daycare attendance, order and number of siblings, and residence in East versus West Germany.

Results. Age-adjusted seroprevalence was 27.4% (95% confidence interval, 25.8–29.0). Cytomegalovirus seroprevalence increased with age (21.5% at ages 1–2; 32.0% at ages 14–17). Cytomegalovirus seropositivity was significantly associated with migration background, country of origin and place of birth, and (among migrants only) with low socioeconomic status. Risk factors for CMV acquisition included the birth order of siblings, breastfeeding, early daycare attendance, and living in East Germany.

Conclusions. In Germany, CMV seroprevalence increases with age, irrespective of gender. These data highlight risk factors associated with seroprevalence and help to identify a target age for the application of a CMV vaccine.

Keywords. children and adolescents; cytomegalovirus; risk factors; seroprevalence; transmission.

Cytomegalovirus (CMV), a member of the *Herpesviridae*, can cause life-threatening disease in immunocompromised individuals as well as in fetuses [1]. The highest risk of transmission and fetal infection occurs if a seronegative mother acquires CMV during pregnancy. This intrauterine transmission can result in microcephaly, mental retardation, developmental delay, visual impairment/retinitis, convulsions, and frequently hearing loss [2]. For Germany, an annual number of 3500 congenitally CMV-infected infants has been estimated [3]. After birth, CMV is transferred from mother to child by breast feeding [4, 5], and CMV immunoglobulin (Ig)G seroprevalence increases with age as children enter daycare facilities. Seropositive children can shed the virus for months and represent a source of infection for seronegative children and caregivers [6–9].

During 2003–2006, the Robert Koch Institute conducted the German Health Interview and Examination Survey for Children and Adolescents (KiGGS) [10]. This nationally representative population-based survey collected data from 16 706 individuals aged 1–17 years. A total of 13 876 sera were tested for CMV IgG antibodies to obtain an estimate of CMV IgG seroprevalence in children and adolescents in Germany. We analyzed the association between CMV seroprevalence and potential factors influencing infection such as household members including siblings, breast feeding, and daycare attendance to identify (1) factors/sources of infection before, during, and after puberty and (2) risk factors for virus transmission that might result in congenital infection.

METHODS

Survey Sample and Design

The KiGGS study is a cross-sectional national health survey among children and adolescents aged 1–17 years living in Germany, conducted by the Robert Koch Institute [10]. Children and adolescents were recruited in 167 sample points (communities) throughout Germany, stratified by federal state and

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community type. Special care was taken to include children and adolescents with a migration background. The overall response rate was 66.6%. Blood samples were collected starting at age 1. The study was approved by the Charité-Universitätsmedizin Berlin ethics committee and the Federal Office for Data Protection.

Serological Testing

Serological testing of CMV IgG in patient samples was performed in the German reference laboratory for measles, mumps, and rubella at the Robert Koch Institute. Cytomegalovirus IgG was evaluated in study subjects older than 1 year to rule out measurement of maternal antibodies.

Cytomegalovirus IgG titer of all serum samples was determined by the Euroimmune anti-CMV-virus-AT-enzyme-linked immunosorbent assay (ELISA) (IgG) (Euroimmun, Luebeck, Germany) based upon lysates from CMV-infected cells. An automated processor (Tecan Evolyzer, Crailsheim, Germany) was used. All samples were tested with kits of the same lot number. The result of the ELISA was calculated by correlation to a standard curve and expressed in relative units (RU)/mL. This result was interpreted according to the manufacturer's recommendations as negative for titers <16 RU/mL, equivocal for titers ≥16 and <22 RU/mL, and positive for titers ≥22 RU/mL.

Variables

Information was collected in self-administered questionnaires filled in by the parents and by the adolescents themselves (starting at age 11). A participant was defined to have a 1-sided/2-sided migration background (MigB) if 1/both of the parents were not born in Germany and/or had no German citizenship [11]. For the present analysis, country of origin was defined to be the country where the mother was born; if this information was missing or the 1-sided MigB was from the father's side, the father's country of birth was used. The country of origin was grouped as follows: Turkey; Russian Federation/former Soviet Union (eg, Lithuania, Ukraine, Belarus, Kasachstan); Central/Southern Europe (eg, Bosnia, Bulgaria, Greece, Spain, Romania); Western Europe etc (eg, Belgium, Denmark, France, Slovakia, Switzerland, Hungary, Canada, Unites States of America, Australia); Poland; Arabic-Islamic countries (eg, Lebanon, Marocco, Pakistan, Senegal, Guinea); other countries (eg, Argentina, Brazil, Vietnam, the Philippines, China, Angola, Eritrea) [12]. In the descriptive analyses, nonmigrants and migrants with a 1-sided MigB were grouped together. The place of birth of the children themselves was taken from the adolescents' questionnaire and classified as Germany yes/no. Children aged 1–10 were assumed to have been born in Germany if the year when the mother migrated to Germany was before the child's birth year, which introduces some uncertainties in very young children. Socioeconomic status (SES) was defined based on the parents' highest educational status, the parents' highest professional status, and household income, and classified into 3 categories [10, 13]. Region was categorized as East Germany (including Berlin) versus West Germany. Sibling order was defined based on siblings living in the same household because this provided somewhat larger associations in preliminary analyses than using the order of biological siblings. Children and adolescents were classified as (1) having no siblings or being a middle child (ie, having both younger and older siblings living in the household), (2) being the oldest child, or (3) being the youngest child in the household. Daycare attendance was categorized based on the age when daycare attendance started (0 or 1 years vs 2 years vs 3 years or older). Breastfeeding was classified as never breastfed versus ever, but not fully breastfed versus ever breastfed with missing information on whether this was full breastfeeding or not versus fully breastfed, but not until the 4th month versus fully breastfed until the 4th month or longer. "Full breastfeeding" means exclusive or predominant breastfeeding, ie, breastfeeding with possible additional intake of water or tea [14].

Statistical Analysis

All analyses were done using the KiGGS sampling weights for the population with a blood sample available. This weight accounted for the unequal sampling probabilities due to the design and included an adjustment to the German population statistics (as of December 31, 2004) by age, sex, region, and nationality (German vs non-German) [10]. In sensitivity analyses, an extended weighting factor was used that additionally adjusted for parental education × MigB. Standard errors were calculated by Taylor linearization and taking the weighting and the clustering in sample points into account, using the survey procedures in SAS version 12.3 (2012; SAS Institute, Cary, NC). Confidence intervals (CIs) were calculated on the logit scale.

A multivariable logistic regression model was built to analyze the association of various factors with CMV IgG seropositivity. Only participants with complete information on all model variables were included in the model. The final model included sex, age group, region, MigB, country of origin, place of birth, SES (low vs medium or high SES), sibling order, daycare attendance, breastfeeding, and the interaction of MigB and SES. Variable selection was done based on the Akaike information criterion and the significance level ($P = .05$). In addition to the adjusted odds ratios (aOR) and their 95% CIs, predictive margins were calculated to give an illustration of the aOR on the prevalence scale. The predictive margins are the averaged probabilities of CMV IgG seropositivity predicted by the model, comparing, eg, East and West Germany and leaving all other variables unchanged [15–17]. Thus, the predictive margins can be thought of as adjusted prevalences reflecting only the effect of the variable in question, in this case region, assuming that all other variables, eg, MigB, show the same distribution across regions. The predictive margin for a particular country of origin was calculated according to the weighted proportion of 1-sided/2-sided

MigB among all migrants. The predictive margins for 1-sided/2-sided MigB were calculated once for Turkey, the reference category of the country of origin, and once for the marginal distribution of the country of origin among all migrants.

RESULTS

Descriptive Analysis

During 2003–2006, 16 706 individuals aged 1–17 years in Germany were interviewed for the KiGGS study. Of these, 13 876 (83%) children and adolescents were screened for CMV IgG antibodies (Table 1).

The overall CMV IgG seroprevalence was 27% (95% CI, 26–29). There was no significant difference in CMV seroprevalence between same-aged boys and girls throughout childhood and teenage years, and seroprevalence increased gradually from infancy to early adulthood (Figure 1). Through all ages, children and adolescents with a 2-sided MigB had significantly higher percentages of CMV IgG antibodies than those without MigB, ranging from 55% in 1- to 2-year-olds to 76% in 14- to 17-year-olds (Figure 2a). The overall prevalence of CMV IgG was 66% (95% CI, 64–69) in individuals with a 2-sided MigB; in contrast, only 19% (95% CI, 18–21) of those without a MigB or with a 1-sided MigB were CMV IgG-positive. A higher prevalence of CMV IgG in children born outside Germany (78%; 95% CI, 74–81) compared with those born in Germany (24%; 95% CI, 23–26) (Figure 2b) was observed. Apart from the youngest age group, where the place of birth could not be ascertained precisely, the increase in CMV IgG seropositivity with age was less pronounced when stratifying on place of birth than when stratifying on MigB. The association of CMV IgG seropositivity with SES differed according to MigB. Migrants with low SES had statistically significantly higher CMV antibody frequencies compared with those with middle or high SES. Nonmigrants or those with a 1-sided MigB with a low SES had lower CMV antibody frequencies than those with middle or high SES (Figure 2c). Overall, CMV IgG seroprevalence was higher among those with a low SES (34%; 95% CI, 32–37) than among those with a middle or high SES (25% and 23%; 95% CI, 23–26 and 21–25) (Figure 2c). Cytomegalovirus IgG seroprevalence changed by at most 2 percentage points when the extended weighting factor was used (results not shown), with the exception of the 1- to 2-year-olds born outside Germany where the prevalence rose from 46% to 53% with the extended weighting factor.

To identify factors associated with CMV seroprevalence, we analyzed different variables in a multivariable logistic regression model that was additionally adjusted for age group ($P < .01$) and sex ($P = .14$) (Table 2). The risk of being CMV seropositive was higher in East Germany (including Berlin) than in West Germany (aOR = 1.38; 95% CI, 1.18–1.63), corresponding to a difference in the average predicted probability of being CMV seropositive of 29% versus 24%.

The odds ratio (OR) for MigB differed by SES (P for interaction = .02). In case of a low SES, the aOR for a 1-sided MigB versus none was 7.95 (95% CI, 5.09–12.4), and the aOR for a 2-sided MigB versus none was 23.9 (95% CI, 17.4–32.8); in case of a middle or high SES, the aOR was lower at 7.22 (95% CI, 4.85–10.7) for a 1-sided and 16.0 (95% CI, 11.3–22.7) for a 2-sided MigB. It should be noted that these OR refer to Turkey as the country of origin, the country with the highest aOR. For other countries of origin, the aOR must be multiplied by the aOR for the respective country; for example, for children and adolescents with a middle or high SES and a 1-sided MigB from Poland, the aOR compared with nonmigrants is $7.22 \times 0.20 = 1.46$.

Table 1. Study Population and CMV IgG Seroprevalence in 1- to 17-Year-Olds by Age Group and Sex, KiGGS Study, Germany 2003–2006

Age	Sex	Total No.	No. With CMV Result	Percent With CMV Result	CMV Seroprevalence (95% CI)
1–2 yrs	Boys	936	535	57%	21.4% (17.5–25.9)
1–2 yrs	Girls	934	523	56%	21.7% (17.5–26.5)
1–2 yrs	Total	1870	1058	57%	21.5% (18.4–25.1)
3–6 yrs	Boys	1950	1486	76%	24.6% (21.9–27.4)
3–6 yrs	Girls	1925	1406	73%	24.6% (21.7–27.7)
3–6 yrs	Total	3875	2892	75%	24.6% (22.3–27.0)
7–10 yrs	Boys	2127	1860	87%	25.8% (23.5–28.3)
7–10 yrs	Girls	2021	1739	86%	25.8% (23.1–28.7)
7–10 yrs	Total	4148	3599	87%	25.8% (23.9–27.8)
11–13 yrs	Boys	1588	1467	92%	28.0% (24.9–31.2)
11–13 yrs	Girls	1488	1382	93%	29.1% (26.3–32.2)
11–13 yrs	Total	3076	2849	93%	28.5% (26.1–31.1)
14–17 yrs	Boys	1904	1775	93%	30.5% (27.9–33.4)
14–17 yrs	Girls	1833	1703	93%	33.5% (30.8–36.3)
14–17 yrs	Total	3737	3478	93%	32.0% (29.9–34.1)
Total	Boys	8505	7123	84%	26.8% (25.1–28.6)
Total	Girls	8201	6753	82%	27.9% (26.1–29.8)
Total	Total	16 706	13 876	83%	27.4% (25.8–29.0)

Abbreviations: CI, confidence interval; CMV, cytomegalovirus; Ig, immunoglobulin; KiGGS, German Health Interview and Examination Survey for Children and Adolescents.

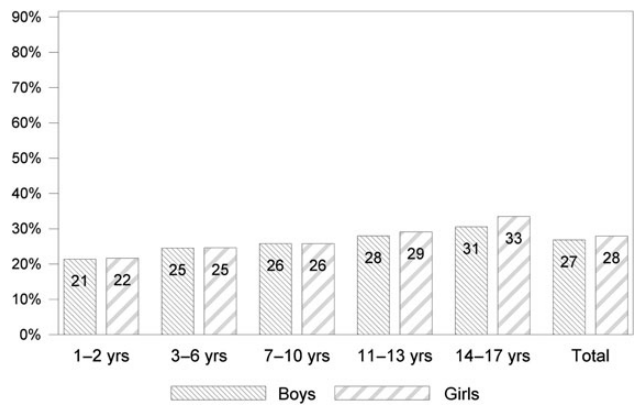

Figure 1. CMV seroprevalence (in percent) in children and adolescents in Germany, by age group and sex (boys left, girls right). In addition, total seroprevalence is shown.

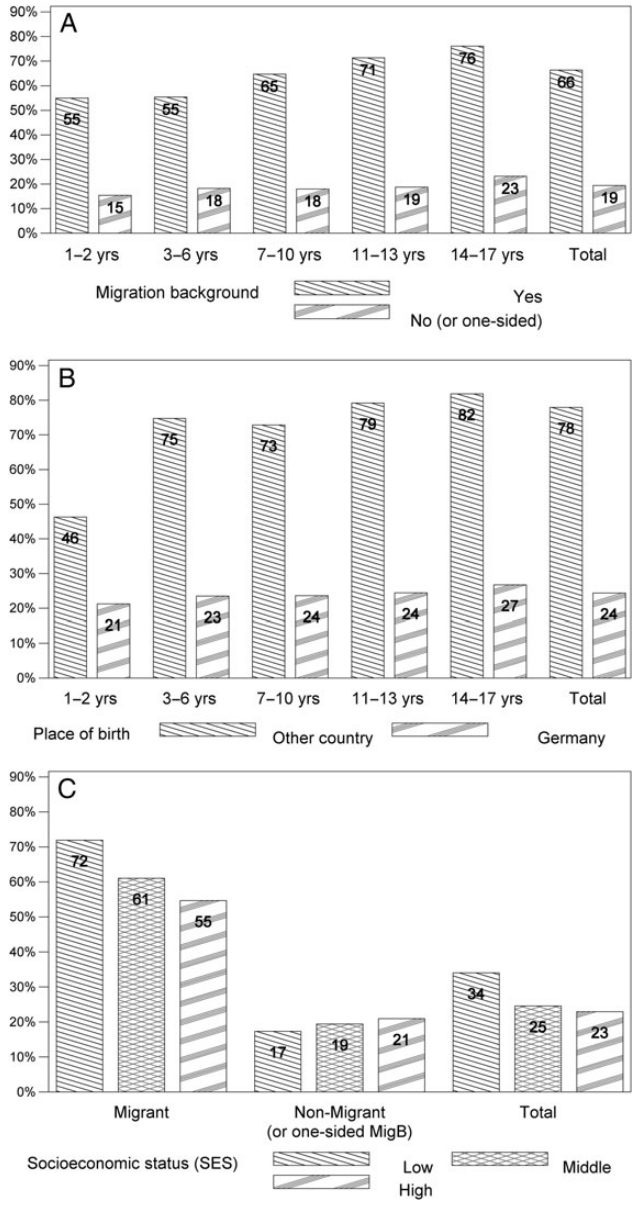

Figure 2. Variables associated with CMV seroprevalence (in percent). For all age groups, CMV seroprevalence is higher in children and adolescents with migration background (A) and if the place of birth was outside Germany (B). In migrants, CMV seroprevalence increases with lower socioeconomic status (SES), which is not observed in non-migrants (C).

The predictive margins were highest for Turkey (70%), Russia and the former Soviet Union (63%), and Arabic-Islamic countries (58%) and lowest for Poland (36%) and Western Europe, North America, etc (21%). For all countries of origin taken together, the predictive margins were 39% for a 1-sided and 61% for a 2-sided MigB, respectively, versus 17% for nonmigrants in case of a low SES. In case of a middle or high SES, the predictive margins were 39% for a 1-sided and 55% for a 2-sided MigB, versus 19% for nonmigrants. The risk for CMV seropositivity was further increased when a child was born outside Germany (aOR = 2.11; 95% CI, 1.51–2.94), corresponding to a predictive margin of 38% (vs 25% for children born in Germany).

An association of SES and CMV seropositivity was only found among children and adolescents with a 2-sided MigB (*P* for interaction = .02), where the aOR for a low SES was 1.35 (95% CI, 1.05–1.73) compared with migrants with a middle or high SES, with predictive margins of 61% and 55%, respectively.

First-born children and adolescents had a higher risk of being CMV seropositive (aOR = 1.36; 95% CI, 1.20–1.54; predictive margin 30%) compared with "middle children" or children and adolescents without siblings (predictive margin 25%). Youngest children, on the other hand, had a lower risk (aOR = 0.77; 95% CI, 0.68–0.86; predictive margin 21%) than those without siblings. When the number of siblings was added to the model, the risk increased by aOR = 1.08 per sibling (*P* = .06), but the protective effect for the youngest child remained unless the number of siblings was 3 or more where the risk was similar to children without siblings (results not shown).

Children enrolled in daycare before the age of 2 had a higher risk for CMV seropositivity with an aOR of 1.35 (95% CI, 1.15–1.59; predictive margin 29%) compared with children who were at home or only attended daycare at 3 years or later (predictive margin 24%). A nonsignificantly elevated aOR of 1.15 (95% CI, 0.95–1.39; predictive margin 26%) was observed when daycare started at age 2.

Finally, breastfeeding increased the risk of being CMV seropositive, with the OR compared with children never breastfed (predictive margin 16%) increasing with the extent and duration of breastfeeding. For children not fully breastfed, the aOR was 1.38 (95% CI, 1.11–1.72; predictive margin 20%), and it increased to aOR = 2.77 (95% CI, 2.35–3.26) and a predictive margin of 30% in children fully breastfed until the 4th month or longer. Sensitivity analyses revealed a further increase in risk when breastfeeding continued until the 6th month or longer (aOR = 2.95 compared with aOR = 2.57 for breastfeeding until the 4th or 5th month). Sensitivity analyses with the extended weighting factor or including missing covariate values as valid values in the model did not change the results appreciably.

DISCUSSION

In our study population of 13 876 children and adolescents, CMV IgG seroprevalence ranged between 21.4% (boys at 1–2 years of age) and 33.5% (girls at 14–17 years of age) with an overall seroprevalence of 27%. For children 1–5 years of age, we detected CMV IgG seroprevalence between 21% and 25%. These results are comparable with data obtained from similar age groups from the National Health and Nutrition Examination Survey (NHANES) of 2011–2012 in the United States (CMV IgG seroprevalence of 20.7%); however, for 1-year-olds, 12.3% was reported for the United States compared with 22% in Germany [18]. Our numbers are higher than those reported for the same age group from a single center 30 years ago [8]. In Germany,

Table 2. Results of Multivariable Logistic Regression Model for CMV IgG Seropositivity in 1- to 17-Year-Olds, KiGGS Study, Germany 2003–2006

Variable	Category	Total No.	No. With CMV Result	Percent With CMV Result	No. in Model	Percent in Model	*P* Value for Variable	*P* Value for Category	aOR[a]	(95% CI)	Predictive Margin
Region	East Germany (including Berlin)	5569	4714	85%	4221	76%	<.01	<.01	1.38	(1.18–1.63)	29%
	West Germany	11 137	9162	82%	8011	72%			Ref.		24%
MigB, stratified by SES[b]	Nonmigrant, low SES	2984	2410	81%	2179	73%	<.01		Ref.		17%
	1-sided MigB, low SES	327	255	78%	203	62%		<.01	7.95[c]	(5.09–12.4)	59%/39% [d]
	2-sided MigB, low SES	1193	950	80%	668	56%		<.01	23.9[c]	(17.4–32.8)	80%/61% [d]
	Nonmigrant, middle/high SES	9865	8370	85%	7935	80%			Ref.		19%
	1-sided MigB, middle/high SES	868	695	80%	594	68%		<.01	7.22[c]	(4.85–10.7)	60%/39% [d]
	2-sided MigB, middle/high SES	1013	831	82%	653	64%		<.01	16.0[c]	(11.3–22.7)	76%/55% [d]
	MigB and/or SES missing	456	365	80%	0						
Country of origin	Turkey	765	591	77%	411	54%	<.01		Ref.		70%
	Russian Fed., former SU	651	538	83%	395	61%		.10	0.70	(0.46–1.07)	63%
	Central/Southern Europe	631	513	81%	387	61%		<.01	0.28	(0.19–0.41)	43%
	Western Europe, USA etc	383	322	84%	307	80%		<.01	0.09	(0.05–0.15)	21%
	Poland	364	315	87%	269	74%		<.01	0.20	(0.13–0.30)	36%
	Arabic-Islamic	295	230	78%	163	55%		<.01	0.55	(0.38–0.79)	58%
	Other	324	252	78%	186	57%		<.01	0.45	(0.28–0.71)	54%
	Missing	481	354	74%	0						
Place of birth	Other country	778	680	87%	431	55%	<.01	<.01	2.14	(1.54–2.96)	38%
	Germany	15 776	13 085	83%	11 801	75%			Ref.		25%
	Missing	152	111	73%	0						
SES, stratified by MigB[b]	Low SES, nonmigrant	2984	2410	81%	2179	73%	.06	.20	0.90	(0.78–1.05)	17%
	Middle/high SES, nonmigrant	9865	8370	85%	7935	80%			Ref.		19%
	Low SES, 1-sided MigB	327	255	78%	203	62%		.98	1.00	(0.64–1.55)	39%[e]
	Middle/high SES, 1-sided MigB	868	695	80%	594	68%			Ref.		39%[e]
	Low SES, 2-sided MigB	1193	950	80%	668	56%		.02	1.35	(1.05–1.73)	61%[e]
	Middle/high SES, 2-sided MigB	1013	831	82%	653	64%			Ref.		55%[e]
	SES and/or MigB missing	456	365	80%	0						
Sibling order	Middle child/no siblings	5404	4474	83%	4149	77%	<.01		Ref.		25%
	Oldest child	4357	3727	86%	3503	80%		<.01	1.36	(1.20–1.54)	30%
	Youngest child	5978	4902	82%	4580	77%		<.01	0.77	(0.68–0.86)	21%
	Missing	967	773	80%	0						
Daycare	Daycare started at age 0 or 1 yrs	2942	2424	82%	2286	78%	<.01	<.01	1.35	(1.15–1.59)	29%
	Daycare started at age 2 yrs	2076	1782	86%	1675	81%		.16	1.15	(0.95–1.39)	26%
	No daycare before age 3	10 702	8903	83%	8271	77%			Ref.		24%
	Missing	986	767	78%	0						

Table 2 continued.

Variable	Category	Total No.	No. With CMV Result	Percent With CMV Result	No. in Model	Percent in Model	*P* Value for Variable	*P* Value for Category	aOR[a]	(95% CI)	Predictive Margin
Breastfeeding	Never breastfed	3531	2905	82%	2620	74%	<.01		Ref.		16%
	Ever (but not fully) breastfed	1299	1106	85%	1013	78%		<.01	1.38	(1.11–1.72)	20%
	Ever breastfed (no info on full breastfeeding given)	1125	953	85%	795	71%		<.01	2.30	(1.81–2.91)	27%
	Fully breastfed (not until the 4th month)	3567	3022	85%	2768	78%		<.01	2.01	(1.69–2.39)	25%
	Fully breastfed at least until the 4th month	6592	5404	82%	5036	76%		<.01	2.77	(2.35–3.26)	30%
	Missing	592	486	82%	0						
Total		16 706	13 876	83%	12 232	73%					25%

Abbreviations: aOR, adjusted odds ratio; CI, confidence interval; CMV, cytomegalovirus; Fed., Federation; Ig, immunoglobulin; KiGGS, German Health Interview and Examination Survey for Children and Adolescents; MigB, migration background; Ref., reference category; SES, socioeconomic status; SU, Soviet Union; USA, United States of America.

[a] Odds ratios adjusted for sex, age group, and all the variables contained in the table.

[b] *P* for interaction migration background; SES = 0.0231.

[c] The aOR refers to country of origin = Turkey. For other countries of origin, the aOR must be multiplied by the aOR for the corresponding country of origin.

[d] The first predictive margin refers to country of origin = Turkey. The second predictive margin refers to the marginal distribution of the country of origin among all migrants with 1-sided or 2-sided migration background.

[e] The predictive margin refers to the marginal distribution of the country of origin among all migrants with 1-sided or 2-sided migration background.

CMV seroprevalence among adolescent females and males aged 11–17 years ranged between 29% and 33% and 28% and 31%, respectively, and are lower than those found in smaller cohorts from the United States [19, 20]. Because this survey was conducted among children and adolescents, no data on maternal CMV serostatus are available, although variations in maternal serostatus are likely to contribute to differences in our subgroups.

Consistent with earlier published NHANES data [21], we found increased CMV IgG seroprevalence in older children, in those with MigB, birth outside Germany, and lower SES. An age-dependent increase in seroprevalence has been documented in several studies [21–27]; however, a study from Norway reported a high regional CMV seroprevalence in young pregnant women [28]. Data from 40 324 pregnant women in Germany showed that seroprevalence of CMV IgG was 42.3% and higher among young women [29]. This might be attributed to increased attendance of daycare facilities and higher rates of breastfeeding but also to different demographics of young pregnant women because unmarried women and women with lower SES or foreign nationality are overrepresented in this group. In a group of 24 260 healthy blood donors in Germany, CMV seroprevalence was reported to be higher in female blood donors with a highest rate of CMV seroconversion in those donors between 30 and 35 years of age [30]. Although these data might not be representative, approximately 30% of live births in Germany are born to women between 30 and 35 years of age, which represents the group with a higher seroconversion rate according to the data from Hecker et al [30], and these women are exposed to their young children. The relatively low level of maternal CMV seroprevalence in Germany is likely to contribute to a lower overall seroprevalence, especially on our cohort of children and adolescents.

In our study, daycare attendance starting before the age of 3 increased the risk of CMV seropositivity. Although this has been reported previously [31, 32], little association between daycare attendance and CMV seroprevalence has been documented by other groups [6, 33–35]. This might be due to the amount of time children spend in the facility at young age but might be influenced by ethnicity and/or household circumstances.

Family members of young children have been reported to be at high risk for CMV infection [36, 37]. This correlates with our finding that the oldest child in a family bears the highest risk of being CMV seropositive and strongly supports that household transmission influences CMV seroprevalence among preadolescent children. Likewise, breastfeeding increased the risk of CMV seropositivity. This is in accordance with data from non-Hispanic white children and Mexican American children with foreign-born parents in the United States [6]. Breastfeeding rates vary by ethnicity and MigB; for example, mothers from Eastern Europe tend to breastfeed their children more frequently and over longer time periods.

In previous studies, African American women caring for young children in the United States have been reported as

being at risk for virus transmission that might result in congenital infection [19]. In our study, children with a 2-sided MigB or those who were born outside Germany had a higher CMV IgG seroprevalence; however, this subgroup represents only a relatively small proportion of the population (approximately 1 in 6 children have a 2-sided MigB). In studies comparing United States-born to non-United States-born children, CMV seroprevalence was shown to be higher in groups with MigB [21]. Immunoglobulin G seroprevalence was only associated with lower SES in children and adolescents with a 2-sided MigB in our cohort. This may be due to the fact that income is more equally distributed in Germany than in other countries, such as Brazil or the United States, so that living conditions are not so disparate among the native German population [38]. On the other hand, this may also reflect the substantial heterogeneity that is present within the migrant population.

The major strength of this study is that it provides nationally representative information on age-specific CMV seroprevalence and determines associated demographic factors. Due to its cross-sectional design, our study cannot clarify the actual onset of CMV infection and only examines variables that were documented at the time of study. Cytomegalovirus seroprevalence in children could not be correlated with the maternal serostatus, and we cannot provide data to identify age groups bearing a higher potential to serve as a source of infection. An evaluation regarding a possible correlation between onset of sexual activity and CMV serostatus is currently under investigation, evaluating whether exposure to young children results more easily in CMV infection than sexual behavior in adolescents, as stated previously [19].

CONCLUSIONS

In conclusion, our data provide important information on CMV seroprevalence in children and adolescents in Germany that might help to assess optimal age for CMV vaccination in a population with overall low CMV seroprevalence. Because young women in their reproductive years are more likely to become infected for the first time and thus are at particular risk of passing the virus to their fetus, they might be considered for interventional studies including vaccine trials. Therefore, these data might be useful on a regional level. However, the rate of CMV seroprevalence varies widely by country or even region, and in countries like Brazil where CMV seroprevalence is already high at young age [39], the data may not be helpful to identify the best target group for vaccination. To determine the latter, individual assessments are necessary.

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