BMC Infectious Diseases

RESEARCH

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Cytomegalovirus and Epstein-Barr virus infections among Jordanians: seroprevalence and associated factors

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Abstract

Background Cytomegalovirus (CMV) and Epstein-Barr virus (EBV) are widespread infections, with seroprevalence rates varying by region and demographic characteristics. This study aimed to examine the seroprevalence of EBV and CMV in the Jordanian population and explore possible risk factors associated with these infections.

Methods A total of 1,507 individuals were recruited through convenience sampling from hospitals located in the central and northern regions of Jordan. Participants were stratified by age, sex, and geographic area. Blood samples were analyzed for EBV-VCA and CMV IgG antibodies using ELISA. Demographic and socioeconomic information was also collected. To identify potential risk factors, multivariate logistic regression was conducted, focusing on variables such as age, sex, marital status, education level, monthly income, region, and type of residence.

Results The overall seroprevalence was 88.7% for CMV-IgG and 91.0% for EBV-IgG. The seroprevalence of both CMV and EBV increased with age from 62.4% and 70.6%, respectively, in children under five years of age to 100.0% and 96.5% in participants aged 60 years and above. Regression analysis indicated that older age and being ever married (i.e., married, divorced, or widowed) were significantly associated with higher seroprevalence of both viruses. Additionally, having a monthly income of 64.3 JD or more per individual was independently linked to higher EBV seroprevalence.

Conclusion EBV and CMV seroprevalence in Jordan was remarkably high. Age was the most prominent risk factor, with marital status and income contributing as independent predictors. These findings offer a valuable reference point for future public health efforts, including surveillance and vaccination strategies targeting high-risk groups.

Keywords Cytomegalovirus, Epstein-Barr virus, Seroprevalence, Jordan, Risk factors

Introduction

Epstein-Barr virus (EBV) and cytomegalovirus (CMV) are two of the most common human herpesviruses. CMV, which belongs to the *Betaherpesvirinae* subfamily, is mainly transmitted through direct contact with bodily fluids such as saliva, urine, and blood [1]. CMV has broad cellular tropism and can infect most organs [2]. In healthy children, primary CMV infections are usually asymptomatic or cause mild symptoms similar to infectious mononucleosis [3]. Like other herpesviruses, CMV undergoes lifelong latency following primary infection and can reactivate later in life [4]. CMV may cause

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serious and life-threatening infections in immunocompromised patients, such as HIV-infected individuals and organ transplant recipients. In these groups, CMV infection may cause hepatitis, encephalitis, pneumonitis, and other complications [5]. Furthermore, CMV is the most common cause of congenital infections and a leading contributor to hearing impairment, vision loss, and developmental abnormalities [6].

Epstein-Barr virus (EBV) belongs to the *Gammaherpesvirinae* subfamily [7]. It is primarily transmitted through direct contact with the oral secretions of an infected person [8]. Once in the oropharynx, EBV enters the lytic cycle, replicating in epithelial cells and shedding into the saliva [9, 10]. EBV can infect B lymphocytes in oral lymphoid tissues and subsequently undergo latency for life in memory B lymphocytes [11]. Most primary EBV infections during childhood are asymptomatic or mild. However, primary infection in late childhood or early adolescence causes symptomatic infectious mononucleosis in approximately half of the cases [12]. Moreover, EBV is classified as a class I carcinogen, as it is responsible for approximately 1–2% of cancer cases worldwide [13]. EBV infection is linked to some malignancies, including Hodgkin lymphoma, non-Hodgkin lymphoma, and nasopharyngeal carcinoma [12]. Infection with EBV has also been linked with autoimmune diseases, including multiple sclerosis, systemic lupus erythematosus, and rheumatoid arthritis (reviewed in [14]).

CMV is highly prevalent worldwide, though its seroprevalence varies considerably across regions and among different socioeconomic and demographic groups. Estimates suggest that CMV seroprevalence ranges from around 40% in some high-income countries to nearly 100% in certain low- and middle-income nations. For instance, the overall CMV seroprevalence in the U.S. population has been reported at 50.4%. Several factors appear to influence seroprevalence, including age, sex, ethnicity, household income, level of education, and household crowding [15]. In France, the overall CMV seroprevalence in the 15–49 year age group was estimated to be 41.9%. The seroprevalence estimates were higher in females and in people born in non-western countries [16]. Higher seroprevalence has been reported in other European countries, including the Netherlands (45.6%), Germany (56.7%), and Croatia (74.4%) [17–19]. High CMV seroprevalence percentages that are close to 100% have been reported in some populations in African countries [20]. In some countries of the Middle East and North Africa (MENA) region, high CMV seroprevalence percentages in selected groups of the population have been reported. For example, the CMV IgG prevalence in blood donors was 92% in Iran and 97.2% in Turkey [21, 22]. In pregnant women in Iran, Turkey, Saudi Arabia, and Egypt, the seroprevalence of CMV was in the range of 95–100% [23–27]. A study from Kirkuk, Iraq, reported an overall CMV seroprevalence of 95.7% in a population of child-bearing-age women [28]. In Jordan, data on CMV seroprevalence remains limited. One study found that among apparently healthy university students aged 18–24 years, CMV seroprevalence was 75.6% in males and 77.2% in females [29].

EBV is also one of the most widespread viral infections worldwide, with an estimated 90% of the world's population having been infected [8]. However, its prevalence varies across geographical regions and age groups. For example, in the United States, EBV seroprevalence ranges from 54.1% among children aged 6–8 years to 82.9% among individuals aged 18–19 years [30]. In the United Kingdom, 85.3% of the population younger than 25 years was seropositive for EBV, with higher seropositivity among older individuals [31]. In Taiwan, EBV seroprevalence was 88.5%, and it increased with age [32]. In addition to age and geographical location, other factors, including ethnicity, educational level, and income, have been reported to influence EBV seroprevalence [30, 32]. EBV seroprevalence has been investigated in some MENA region countries. In a large-scale epidemiological study in Bahrain from 2001–2015, 86.1% of the study population was positive for EBV antibodies, and the trend of seropositivity progressively increased over the period of the study [33]. A high EBV seroprevalence of 97.9% was reported among healthy blood donors from diverse nationalities residing in Qatar [34]. In Tehran province, Iran, the seroprevalence of EBV ranged from approximately 50% in children under the age of 3 years to 94.8% in adults above the age of 40 years [35]. In Jordan, EBV seropositivity has been reported at 96% among patients with multiple sclerosis and 98% among healthy controls [36]. Another study found a seropositivity percentage of 95.1% among Jordanian blood donors residing in Qatar [34].

Despite these findings, data on the seroprevalence of EBV and CMV in Jordan and across the broader MENA region remain scarce. Most existing studies were limited by small sample sizes and the focus on specific subpopulations. Moreover, they often excluded key age groups and geographic regions. In light of the limited population-level data and the substantial health burden posed by these two viruses, this study aimed to provide nationally representative seroprevalence estimates by surveying the general population in northern and central Jordan. The study covered all age groups in the central and northern regions of Jordan, where more than 92% of the Jordanian population resides [37]. In addition, this study investigated the socioeconomic and demographic

risk factors that may influence EBV and CMV seropositivity in Jordan.

Methods

Sample and recruitment

Between December 2021 and August 2022, participants were recruited from seven governmental hospitals and one university hospital located across Jordan's four central governorates (Amman, Zarqa, Balqa, and Madaba) and four northern governorates (Irbid, Mafraq, Jerash, and Ajloun). Recruitment took place among individuals visiting hospital laboratories for routine checkups. The sampling frame included Jordanian nationals who attended these facilities and provided informed consent to participate. Participants who self-reported being immunocompromised, as well as children under one year of age, were excluded from the study.

Demographic information, including age, sex, place of residence, marital status, education level, total household income, and family size, was collected through a structured questionnaire administered to each participant. The questionnaire was specifically developed for this study and written in Arabic. An English translation is provided in the supplementary materials.

Sample size

The following formula was used to estimate an adequate sample size for the current study: $n = Z^2P(1-P)/d^2$. where n is the sample size, Z is the level of confidence, P is the expected prevalence according to the literature, and d is the precision [38].

The global estimated prevalence of CMV and EBV is around 50%. Based on this, the literature recommends using a 5% margin of precision when the expected prevalence falls between 10 and 90%, along with a 95% confidence level [39]. Following these guidelines, the minimum required sample size was calculated to be 730. However, to improve the accuracy of the estimates, detect potential outliers, and reduce the margin of error, the study aimed to recruit over 1,500 participants.

The sample was proportionally stratified by sex, age group, and geographic region. Stratum sizes were determined using data from Jordan's 2020 national census [37].

Blood sample collection

Venous whole blood samples were collected using plain vacutainer tubes. After collection, the blood was centrifuged to separate the serum, which was then divided into at least four microcentrifuge tubes per sample. All serum samples were stored at −80°C until they were ready for analysis.

Serological analysis

Serum samples were thawed at room temperature, and each sample was tested for CMV-specific IgG and EBV-viral capsid antigen (VCA)-specific IgG antibodies. The assays for CMV-IgG and EBV-VCA-IgG antibodies were performed using commercially available ELISA kits (DIA. PRO Diagnostic Bioprobes Srl, Milano, Italy), following the manufacturer's instructions. All recommended quality controls were utilized. Quantitative results for CMV-IgG were expressed in World Health Organization international units per milliliter (WHO IU/mL) for each sample. These values were determined using a standard curve based on the kit's standards, which were calibrated against the First WHO International Standard for anti-CMV IgG (document BS/95.1814). A CMV-IgG result above 0.5 WHO IU/mL was considered positive, while values below this threshold were considered negative. Similarly, quantitative EBV-VCA-IgG results were determined using a standard curve based on the kit's standards. However, due to the lack of an international standard for EBV-VCA-IgG, these results were expressed in arbitrary units per milliliter (arbU/mL), as defined by the manufacturer. EBV-VCA-IgG levels greater than 5 arbU/mL were considered positive, while values below this cut-off were considered negative. Both assays demonstrated sensitivities and specificities exceeding 98%.

Statistical analysis

The data were analyzed using the Statistical Package for the Social Sciences (SPSS) software version 26 (IBM Inc., Armonk, New York, United States). Descriptive statistics, including frequency, mean, median, standard deviation (SD), and range, were used to calculate prevalence percentages and describe the characteristics of the study sample. To assess the significance of differences in seroprevalence across demographic groups, bivariate analysis with a chi-square test was performed. Multivariate analysis, specifically logistic regression, was used to identify risk factors for EBV and CMV infections. An alpha level of ≤ 0.05 was considered statistically significant, and p-values were reported for all comparisons.

Results

A total of 1,507 participants were recruited for this study, following the established sampling criteria. Approximately two-thirds (68.7%) of the study sample were from the central governorates, while one-third (31.3%) were from the northern governorates. The mean age of the participants was 25.6 years (SD = 18.2). The sample included 890 adults (59.1%) aged 18 years

Table 1 Demographic characteristics of the study sample

Characteristic	Frequency (%)
Sex	
Male	792 (52.6%)
Female	715 (47.4%)
Region	
Central Jordan	1035 (68.7%)
Northern Jordan	472 (31.3%)
Age in years (mean ± SD)	25.6 ± 18.2
Less than 5	170 (11.3%)
5–9	182 (12.1%)
10–14	164 (10.9%)
15–19	147 (9.8%)
20–29	285 (18.9%)
30–39	216 (14.3%)
40–49	163 (10.8%)
50–59	95 (6.3%)
60 or more	85 (5.6%)
Employment	
Employed	380 (25.2%)
Unemployed	1127 (74.8%)
Marital status	
Never married	890 (59.1%)
Ever married (married, divorced, widowed)	617 (40.9%)
Type of residency	
Urban	1236 (82.0%)
Rural	271 (18.0%)
Educational level	
High school or below	1189 (78.9%)
College or higher	318 (21.1%)
Household size [median (range)]	6 (1–16)
5 or less members	733 (48.6%)
6 or more members	774 (51.4%)
Monthly income/individual [Median (range)]	64.3 (0.0—1166.7)
Less than 64.3 JD	750 (49.8%)
64.3 JD or more	757 (50.2%)

JD Jordanian Dinar, *SD* Standard deviation

or older and 617 children (40.9%). The sample was stratified into nine age groups, with the number of participants in each group based on national population ratios (Table 1).

Around one-quarter (25.2%) of the participants were employed, 40.9% were currently or previously married, and 21.1% had a college degree or higher. However, these statistics do not reflect the overall employment, marriage, or education rates in the Jordanian population, as they were calculated for the entire sample, including children. The number of household members among participants ranged from 1 to 16, with a median of 6. The median monthly income per household member was 64.3 Jordanian Dinars (JD). A summary of the study sample's characteristics is provided in Table 1.

The seroprevalence of CMV and EBV was first calculated for the entire study sample. A total of 1,337 participants (88.7%) were seropositive for CMV-IgG, while 1,372 participants (91.0%) were seropositive for EBV-VCA-IgG antibodies. Among adult participants, the CMV seroprevalence was 96.1%, and the EBV seroprevalence was 96.7%. To estimate the risk of congenital CMV infections, the CMV seroprevalence among females of childbearing age (18–48 years) was specifically examined. The analysis revealed that, among the 322 female participants in this age group, 313 (97.2%) were positive for CMV-IgG.

The study also explored the effects of various demographic factors on the seroprevalence of both viruses. The sample was stratified into demographic groups, and seropositivity was compared across these groups. CMV-IgG seropositivity was not significantly higher in females (89.8%) compared to males (87.8%). Similarly, there was no significant difference in EBV-VCA-IgG seropositivity between males (91.2%) and females (90.9%) (Table 2).

The influence of region and type of residence on seroprevalence was examined by comparing seropositivity between participants from central and northern governorates, as well as between those from rural and urban areas. No significant differences were observed for either virus across these groups (Table 2).

The impact of age on CMV seroprevalence was assessed by comparing seropositivity across different age groups. The results showed a significant increase ($p < 0.001$) in seropositivity with age. The lowest seroprevalence (62.4%) was observed in children under 5 years, with seropositivity steadily increasing until it reached 100% among participants aged 60 years and older (Table 2). Similarly, EBV-VCA-IgG seropositivity also increased significantly with age ($p < 0.001$) (Table 2). The lowest seropositivity for EBV-VCA-IgG (70.9%) was among children under 5 years, while the highest (98.8%) was among the 40–49-year-old age group. Interestingly, slightly lower seropositivity percentages were noted in the 50 + age groups (Table 2).

To examine the effect of income, participants were divided into two groups based on their monthly income: those earning less than 64.3 JD and those earning 64.3 JD or more, with the cutoff set at the median individual monthly income for the sample. No significant difference in CMV-IgG seroprevalence was found between the high-income and low-income groups (90.0% vs 87.5%, respectively, $p = 0.118$). However, significantly higher EBV-VCA-IgG seropositivity was observed in the low-income group compared to the high-income group

Table 2 CMV and EBV seroprevalence rates according to demographic group

Characteristic	CMV-IgG seropositivity Number (%)	*P* value	EBV-VCA-IgG seropositivity Number (%)	*P* value
Total	1337 (88.7%)		1372 (91.0%)	
Sex		0.212		0.864
Male	695 (87.8%)		722 (91.2%)	
Female	642 (89.8%)		650 (90.9%)	
Region		0.966		0.359
Central Jordan	918 (88.7%)		947 (91.5%)	
Northern Jordan	419 (88.8%)		425 (90.0%)	
Type of residency		0.173		0.114
Urban	1103 (89.2%)		1132 (91.6%)	
Rural	234 (86.3%)		240 (88.6%)	
Age group		< 0.001*		< 0.001*
Less than 5	106 (62.4%)		120 (70.6%)	
5–9	140 (76.9%)		154 (84.6%)	
10–14	143 (87.2%)		149 (90.9%)	
15–19	134 (91.2%)		131 (89.1%)	
20–29	269 (94.4%)		270 (94.7%)	
30–39	209 (96.8%)		212 (98.1%)	
40–49	158 (96.9%)		161 (98.8%)	
50–59	93 (97.9%)		93 (97.9%)	
60 and more	85 (100%)		82 (96.5%)	
Monthly income/individual		0.118		0.002*
Less than 64.3 JD	662 (87.5%)		706 (93.3%)	
More than 64.3 JD	675 (90.0%)		666 (88.8%)	
Household size		0.482		0.132
5 or less members	646 (88.1%)		659 (89.9%)	
6 or more members	691 (89.3%)		713 (92.1%)	

* $p < 0.05$, chi-square test

(93.3% vs 88.8%, respectively, $p = 0.002$). The study also divided participants based on the number of household members, categorizing them into two groups: those with 5 or fewer members and those with 6 or more. However, no significant differences in CMV-IgG or EBV-VCA-IgG seropositivity were found between these groups (Table 2).

Employment status, educational level, and marital status are largely influenced by age, as children and young adults are less likely to have completed higher education, be married, or be employed. To more accurately assess the effects of these factors on CMV-IgG and EBV-VCA-IgG seroprevalence, the analysis was limited to 691 participants aged 25 years or older. Among these participants, 97.5% were seropositive for both CMV-IgG and EBV-VCA-IgG. Notably, a higher prevalence of CMV-IgG was found in females compared to males (99.4% vs 95.9%, respectively, $p = 0.003$), and in unemployed participants compared to employed participants (98.9% vs 96.1%, respectively, $p = 0.019$). In contrast, there were no significant differences in EBV-VCA-IgG seropositivity between males and females, or between employed and unemployed participants (Table 3). EBV-VCA-IgG seropositivity was significantly higher in ever-married participants compared to never-married participants (98.4% vs 93.3%, respectively, $p = 0.001$), while no significant differences in CMV-IgG seropositivity were observed between these groups. Lastly, no significant differences in seropositivity for either virus were found between the different educational level groups (Table 3).

A multivariate logistic regression analysis was conducted to identify independent risk factors for CMV infection and to account for potential confounding variables. The analysis included sex, age group, region, residency, monthly income, number of household members, educational level, employment, and marital status. After adjustment, older age and being ever married (married, divorced, or widowed) were identified as significant predictors of a higher risk of CMV infection (Table 4). The risk of infection increased progressively with age. For example, the risk for the 5–9-year age group was

Table 3 CMV and EBV seroprevalence in the demographic groups of adults aged 25 years or older

Characteristic	Number of participants (> 25 years)	CMV-IgG seropositivity Number (%)	*P* value	EBV-VCA-IgG seropositivity Number (%)	*P* value
Sex			0.003*		0.641
Male	368	353 (95.9%)		358 (97.3%)	
Female	323	321 (99.4%)		316 (97.8%)	
Educational Level			0.212		0.468
High school or below	463`	454 (98.1%)		453 (97.8%)	
College or higher	228	220 (96.5%)		221 (96.9%)	
Employment status			0.019*		0.388
Employed	335	322 (96.1%)		325 (97.0%)	
Unemployed	356	352 (98.9%)		349 (98.0%)	
Marital status			0.184		0.001*
Never married	120	115 (95.8%)		112 (93.3%)	
Ever married	571	559 (97.9%)		562 (98.4%)	

* $p < 0.05$, chi-square test

Table 4 Results of the multivariate logistic regression analysis for predicting the risk factors for CMV infection

Variable	Category	*P* value	Adjusted odds ratio (95% CI)
Sex	Female		Reference
	Male	0.368	0.848 (0.593—1.214)
Age group (years)	Less than 5		Reference
	5–9	**0.003**	2.035 (1.268—3.266)
	10–14	**< 0.001**	4.291 (2.402—7.663)
	15–19	**< 0.001**	6.926 (3.484—13.770)
	20–29	**< 0.001**	12.312 (5.239—28.935)
	30–39	**< 0.001**	12.841 (3.776—43.663)
	40–49	**0.001**	11.296 (2.762—46.193)
	≥ 50	**< 0.001**	29.587 (5.145—170.137)
Region	Northern Jordan		Reference
	Central Jordan	0.675	0.914 (0.600—1.392)
Residency	Rural		Reference
	Urban	0.498	1.177 (0.734—1.889)
Monthly income (JD)	< 64.3		Reference
	≥ 64.3	0.370	1.190 (0.814—1.739)
Household size	< 6 members		Reference
	≥ 6 members	0.912	0.978 (0.659—1.451)
Educational level	High school or below		Reference
	College or higher	0.161	0.610 (0.306—1.217)
Employment status	Unemployed		Reference
	Employed	0.266	0.652 (0.307—1.384)
Marital status	Never married		Reference
	Ever married	**0.038**	2.799 (1.059—7.398)

approximately twice that of children under 5 years old [aOR = 2.035 (95% CI: 1.268–3.266)]. However, the risk of infection was more than 29 times greater in the participants aged ≥ 50 years compared to young children [aOR = 29.587 (95% CI: 5.145–170.137)] (Table 4). Additionally, being currently or previously married increased the risk of CMV infection nearly threefold [aOR = 2.799 (95% CI: 1.059–7.398)].

Similarly, multivariate logistic regression was performed to examine the risk factors for EBV infection. Consistent with the results for CMV, older age groups were associated with an increased risk of EBV infection (Table 5). Moreover, current or previous marriages were associated with nearly three times the risk of EBV infection compared to never-married individuals [aOR = 3.118 (95% CI: 1.173–8.289)]. In contrast, having a monthly income above 64.3 JD was associated with a lower risk of EBV infection than being in the lower income group [aOR = 0.439 (95% CI: 0.290–0.665)] (Table 5).

Discussion

CMV and EBV, both members of the *Herpesviridae* family, are among the most widely prevalent viruses worldwide. Numerous studies have shown that their seroprevalence varies across different regions and demographic groups. This study offers valuable data on the seroprevalence of CMV and EBV in the central and northern governorates of Jordan, where most of the population resides. In addition, it investigates potential demographic risk factors for infection by the two viruses.

The overall seroprevalence of CMV in this study was 88.7%, which is significantly higher than the reported CMV seroprevalence in several industrialized countries, including the USA [15], France [16, 40], Germany [19, 41], and the Netherlands [17]. The CMV seroprevalence among adults was very high (96.1%) in the current study, which is consistent with reported seroprevalence percentages in adults from several Asian, African, or South American countries, including India [42], Pakistan [43], Tunisia [44], Kenya [45], Somalia [46], and Brazil [47]. Compared to other Middle Eastern countries, the CMV seroprevalence in adults in this study was higher than that in adults from Iran (92%), but slightly lower than that in adults from Turkey (97.2%) [21, 22]. Among female participants of childbearing age, 97.2% were positive for CMV-IgG in this study. This result is in line with the reported high seroprevalence percentages in the region, such as among Syrian refugees and Iraqi women, but was significantly higher than that from industrialized countries such as Germany, and among women of childbearing age [28, 41].

The overall EBV seroprevalence in the study sample was 91.0%. The national estimates of EBV seroprevalence are scarce in the literature. In Bahrain, an EBV seroprevalence of 86.1% was reported, which is in line with the current study [33]. Similarly, a study from Taiwan reported a

Table 5 Results of the multivariate logistic regression analysis for predicting the risk factors for EBV infection

Variable	Category	*P* value	Adjusted odds ratio (95% CI)
Sex	Female		Reference
	Male	0.734	1.070 (0.724—1.583)
Age group (years)	Less than 5		Reference
	5–9	**0.004**	2.186 (1.281—3.732)
	10–14	**< 0.001**	3.771 (1.960—7.256)
	15–19	**0.001**	2.959 (1.530—5.722)
	20–29	**< 0.001**	5.049 (2.139—11.920)
	30–39	**0.001**	9.607 (2.412—38.267)
	40–49	**0.006**	12.081 (2.051—71.146)
	≥ 50	**0.026**	4.597 (1.203—17.566)
Region	Northern Jordan		Reference
	Central Jordan	0.955	1.013 (0.645—1.592)
Residency	Rural		Reference
	Urban	0.394	1.247 (0.751—2.069)
Monthly income (JD)	< 64.3		Reference
	≥ 64.3	**< 0.001**	0.439 (0.290—0.665)
Household size	< 6 members		Reference
	≥ 6 members	0.781	0.941 (0.611—1.449)
Educational level	High school or below		Reference
	College or higher	0.171	1.717 (0.791—3.724)
Employment status	Unemployed		Reference
	Employed	0.629	0.818 (0.363—1.845)
Marital status	Never married		Reference
	Ever married	**0.023**	3.118 (1.173—8.289)

seroprevalence of 88.5% [32]. The seroprevalence values for the different age groups were comparable between our study and the Taiwanese study. In our study, participants aged 25 years or younger had an EBV seroprevalence of 85.7%, which aligns with the reported 85.3% in the same age group in the UK [31]. In contrast, the EBV seroprevalence in the 6–19-year age group in the USA was lower than the values reported in the same age group in our study [30].

As anticipated, our results demonstrated that age was the most significant factor influencing CMV seroprevalence. Seroprevalence increased during childhood, reaching 91.2% in the 15–19-year age group, with further increases observed in adulthood. These findings align with trends reported in other studies. For instance, a study from the USA found that CMV seroprevalence rose from 37.5% in the 6–11-year age group to 42.7% in the 12–19-year age group [15]. A second study reported a CMV IgG seroprevalence of 20.7% among young children aged 1–5 years in the USA [48]. In Croatia, CMV IgG seroprevalence increased from 53% in the 6 months—9 years age group to 55.4% in the 10–19-year age group and increased further with increasing age [18]. CMV seroprevalence percentages were higher among the age groups in our study than among similar age groups in the USA or Croatia. Age was also the main factor influencing the EBV seroprevalence. The EBV seroprevalence increased from 70.6% in children under 5 years of age to 89.1% in adolescents aged 15–19 years. Furthermore, the EBV seroprevalence increased at a slower rate in adult age groups. These results are in line with those reported in the USA and Taiwan. However, seroconversion rates in Jordanian children were faster than those reported in children from the USA but slower than those reported in Taiwan [32, 49]. The differences in the seroprevalence percentages for the two viruses between this study and other studies could be attributed to cultural factors influencing intimate contact within the community, including interactions between mothers and children, as well as variations in population density between countries.

After adjusting for potential confounders, marital status emerged as an independent risk factor for both CMV and EBV infections. Multivariate logistic regression analysis revealed that individuals with a history of marriage (married, divorced, or widowed) were approximately three times more likely to test positive for CMV and EBV compared to never-married participants. Consistent with these findings, univariate analysis showed a significantly higher CMV seroprevalence among married individuals in Pakistan compared to their unmarried counterparts [43]. In contrast, marital status was not associated with the EBV seroprevalence in Taiwan [32]. Marriage may increase the risk of CMV and EBV infection due to sexual contact between partners. This association is particularly relevant in conservative and religious societies, such as many Middle Eastern countries, including Jordan, where premarital intimate contact is generally limited due to religious and cultural constraints. In such communities, marriage often marks the onset of sexual activity, potentially facilitating the transmission of these viruses. In contrast, in less conservative or more secular societies, marriage may be linked to a reduction in the number of lifetime sexual partners, which could offer a protective effect against viral transmission. Studies in the USA have shown that both sexual activity and the number of lifetime sexual partners are associated with CMV seropositivity [50, 51].

Multivariate analysis identified income as an independent risk factor for EBV seropositivity but not for CMV seropositivity. Participants with a monthly income of 64.3 JD (approximately 90.6 USD) or more had less than half the odds of being EBV seropositive compared with those with lower incomes [aOR = 0.439 (95% CI: 0.290—0.665)]. In agreement with this, a higher household income was associated with significantly lower EBV seroprevalence among individuals aged 6–19 years in the USA [30, 49]. Income can influence the risk of infection in many ways. For example, children from higher-income families are more likely to attend private schools, which typically have smaller class sizes compared to public schools attended by the majority of low-income children.

Although univariate analysis revealed a significantly higher CMV seroprevalence in females compared to males in the >25 years age group (Table 3), this difference was not significant after adjusting for confounding factors in multivariate analysis (Table 4). In contrast, an association between female sex and a higher risk of CMV seropositivity has been observed in other countries, including France, Pakistan, the USA, and Canada [15, 16, 43, 52]. This discrepancy could be partly attributed to cultural differences between Jordan and these countries, which influence the social and professional interactions of females with other members of the community. Similarly, univariate analysis revealed a higher CMV seroprevalence among unemployed adult participants (> 25 years) than among employed participants. However, this difference was not significant after adjusting for confounding factors. Notably, in our study sample, there were significantly higher unemployment rates among adult female participants than among male participants (81.4% vs. 25.3%, respectively). Finally, no significant associations were found between CMV or EBV seroprevalence and education level, region or nature of the residency place, or household size.

This study provides valuable data on the prevalence and risk factors for CMV and EBV in Jordan, an understudied

population. These findings serve as a baseline for future studies monitoring the prevalence and transmission trends of these viruses in Jordan and could offer a useful reference for neighboring countries in the MENA region. Such data are crucial for public health policymakers, enabling them to identify high-risk groups for targeted interventions and preventive measures. This approach could reduce the burden of CMV and EBV on public health, especially among vulnerable and susceptible populations. While no approved vaccines for EBV or CMV are currently available, several vaccine candidates are under investigation. Once these vaccines become available, effective distribution strategies should aim to minimize the community burden of these viruses. These strategies require a precise understanding of the epidemiology and risk factors for EBV and CMV, as identified in this study.

However, this study has some limitations. Firstly, the sample covered the central and northern governorates of Jordan but did not include the southern governorates. Although over 92% of Jordanians reside in the central and northern regions, including the southern governorates would have provided a more comprehensive understanding of the prevalence of these viruses across the entire country. The population density in the southern regions is significantly lower than in the central and northern regions, which could influence viral prevalence, as higher population densities are often associated with higher transmission rates. Additionally, this study focused on the seroprevalence of viral IgG antibodies and did not assess IgM antibodies. Including IgM antibodies would have detected participants in the earlier stages of infection before IgG antibodies become detectable. However, since IgG antibodies are long-lasting and IgM antibodies are transient, relying on IgG detection alone is unlikely to result in significant underestimation of the seroprevalence percentages.

Conclusion

In conclusion, this study found very high seroprevalence percentages for CMV and EBV in the populations of central and northern Jordan. More than half of the population had acquired these infections by the age of five, with seroprevalence continuing to increase with age. Being married was associated with higher odds of CMV and EBV seropositivity. Having a higher income was linked to lower odds of EBV seropositivity. While no significant association was found between income and CMV seropositivity. Other factors, such as educational level, household size, employment status, and place of residence (urban vs. rural or central vs. northern), did not show a significant association with the seroprevalence of either virus.

Abbreviations

aOR	Adjusted odds ratio
arbU	Arbitrary units
CI	Confidence interval
CMV	Cytomegalovirus
EBV	Epstein–Barr Virus
ELISA	Enzyme-linked immunosorbent assay
HIV	Human immunodeficiency virus
IgG	Immunoglobulin G
IgM	Immunoglobulin M
IRB	Institutional Review Board
IU	International unit
JD	Jordanian Dinars
MENA	Middle East and North Africa
mL	Milliliter
SD	Standard deviation
UK	United Kingdom
USA	United States of America
USD	United States dollar
VCA	Viral capsid antigen
WHO	World Health Organization

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12879-025-11110-2.

Supplementary Material 1.

Acknowledgements

The authors would like to acknowledge the Deanship of Research at Jordan University of Science and Technology for providing financial support for this project (Grant number 20210234) and administrative support. We also extend our gratitude to the Jordanian Ministry of Health for facilitating sample collection. Finally, we would like to express our appreciation to Dr. Maria Obeidat and Dr. Mohammad Al Shboul for their valuable support.

Clinical trial number

Not applicable.

Authors' contributions

Conceptualization: HMK. Methodology: HMK, SFS, MJ. Laboratory analysis: HMK, SFS. Statistical Analysis: HMK, MJ. Validation: HMK, SFS, MJ. Writing – original draft: HMK. Writing – review & editing: SFS, MJ.

Funding

This work was supported by the Deanship of Research at Jordan University of Science and Technology [Grant number 20210234].

Data availability

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

The study was approved by the institutional review board (IRB) of Jordan University of Science and Technology (Ref: 8/140/2021, date 28.04.2021) and the ethics committee of the Jordanian Ministry of Health (Ref: Moh/REC/2021/131, date 26.07.2021) before the recruitment of study participants. Written informed consent was obtained from each adult participant. A parent or legal guardian for child participants was required to complete a written informed consent form before participation. This study was conducted in accordance with the Declaration of Helsinki.

Consent for Publication:

Not applicable.

Competing interests

The authors declare no competing interests.

Received: 15 March 2025 Accepted: 13 May 2025
Published online: 21 May 2025

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