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ORIGINAL ARTICLE

Cytomegalovirus Seroprevalence in Morocco - a 10-Year Single-Center Study

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SUMMARY

Background: **Cytomegalovirus is a ubiquitous and endemic virus, typically causing asymptomatic or mild infections in immunocompetent individuals. However, it can lead to severe disease in immunocompromised patients and during congenital infections. The objective of this study was to determine the seroprevalence of CMV in a Moroccan population.**
Methods: **We conducted a retrospective, cross-sectional study at the Central Virology Laboratory of the Specialties Hospital in Rabat over a 10-year period, from April 1, 2015, to December 31, 2024.**
Results: **A total of 11,367 patients who underwent CMV serological testing were included. The overall CMV seroprevalence was 94.1%. The median age of seropositive individuals was significantly higher than that of seronegative individuals (26 [9;45] years vs. 3 [1;8] years; $p < 0.001$). Seroprevalence was found to increase significantly with age (74.0%, 83.0%, 91.9%, 95.6%, and > 97.7% in children under 2 years of age, and in those aged 2 - 5, 6 - 10, 11 - 16, and > 17 years, respectively; $p < 0.001$). Despite an increase in the number of testing requests over the study period, the annual seroprevalence remained stable, ranging from 92.2% to 95.7%.**
Conclusions: **These findings indicate that CMV seroprevalence in Morocco is high and aligns with rates observed in other developing countries.**
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INTRODUCTION

Human cytomegalovirus (CMV) or HHV-5 is a virus that belongs to the *Herpesviridae* family and is classified in the *Betaherpesvirinae* subfamily [1]. Its prevalence varies from 50% to 100%, depending on age, country, and the socioeconomic level of the population [1]. It is a double-stranded DNA virus with an envelope, characterized by multiple latency sites [1,2]. After the primary infection (PI), the virus remains latent in the body for life, with the potential for secondary infections - either endogenous (reactivations) or exogenous

(reinfections) [2].
Human cytomegalovirus is an opportunistic infectious agent that is typically benign in immunocompetent individuals but can have severe consequences in immunocompromised patients or in fetuses [1,2]. Indeed, congenital cytomegalovirus infection is the leading cause of infectious embryofetopathy and is a cause of motor deficits and neurosensorial hearing loss, second only to genetic causes [3,4]. The illness occurs mainly in cases of PI in pregnant women, but also in cases of reactivation or secondary infection [5]. As a result, many studies have focused on these groups of patients.
In Morocco, CMV infections remain underdiagnosed, with diagnostic efforts primarily developed in kidney transplant recipients. Similarly, there is no national data on the seroprevalence of this infection.
The aim of our study is to determine the seroprevalence of CMV based on data from the Central Virology Laboratory of Ibn Sina University Hospital in Rabat.

MATERIALS AND METHODS

Study setting
This is a retrospective cross-sectional study conducted at the Central Virology Laboratory of the Specialties Hospital in Rabat over a 10-year period, from April 1, 2015, to December 31, 2024. All patients who were hospitalized or seen as outpatients at the various hospitals of Ibn Sina University Hospital in Rabat and who underwent qualitative and quantitative testing for anti-CMV IgG antibodies were included in the study.
Exclusion criteria included samples from infants under 6 months of age (due to the persistence of maternal IgG), samples from children whose age was not specified in the test request, and uncertain or equivocal results.

Clinical specimens
The received samples were collected in dry tubes, with or without a separating gel. Upon receipt, the tubes were centrifuged at 4,000 r/minute for 15 minutes before processing.

CMV serological assays
All received samples underwent qualitative and/or quantitative detection of anti-CMV IgG antibodies using a microparticle immunoassay by chemiluminescence (CMIA) on the Abbott Architect or Abbott Alinity i analyzers. The positivity threshold for anti-CMV IgG antibodies was an index ≥ 6.0 AU/mL according to the manufacturer's instructions.

Statistical analysis
All statistical analyses were performed using Jamovi software, version 2.5. Descriptive statistics were used to summarize the data. Quantitative variables were expressed as means with standard deviations or as medians with interquartile ranges, depending on the distribution. Qualitative variables were presented as absolute counts and percentages. Comparisons of quantitative variables between two independent groups were conducted using the Student's *t*-test for normally distributed data, and the Mann-Whitney U test for non-normally distributed data. Associations between categorical variables were assessed using the chi-squared test or Fisher's exact test, as appropriate. A p-value of less than 0.05 was considered statistically significant.

RESULTS

Characteristics of the studied population
During the study period, 11,367 patients were included. The median age of the study population was 24 [7;43] years, and the male-to-female (M/F) gender ratio was 0.87. A total of 4,110 patients (36.2%) were children, with a median age of 5 [2;10] years and a gender ratio M/F of 1.27, while 7,257 patients (63.8%) were adults, with a median age of 40 [29;56] years and a gender ratio M/F of 0.70.
The number of requests received by the Central Virology Laboratory increased steadily each year, rising from 558 in 2015 to 2,152 in 2024. The annual distribution of requests is shown in Figure 1.

CMV prevalence in the studied population
Of the 11,367 patients included in our study, 10,698 tested positive for anti-CMV IgG antibodies, corresponding to an overall seroprevalence of 94.1%. Seroprevalence was significantly higher in females (95.2% vs. 92.9% in males; $p < 0.001$), in adults (98.5% vs. 86.4% in children; $p < 0.001$), and it increased significantly with age ($p < 0.001$) (Figure 2).
The median age of seropositive patients was 26 [9;45] years compared to 3 [1;8] years for seronegative patients ($p < 0.001$). Furthermore, despite the increase in the number of requests received between 2015 and 2024, the overall seroprevalence remained stable, ranging from 92.2% to 95.7% (Figure 1).

CMV seroprevalence in children
Among the 4,110 children included in our study, 3,553 had a positive CMV IgG serology, corresponding to an overall seroprevalence of 86.4%. The median age of this group was significantly higher than that of seronegative patients (6 [3;11] years vs. 2.5 [1;5] years, respectively; $p < 0.001$). No statistically significant difference was observed according to gender ($p = 0.500$). The seroprevalence rates were as follows: 91.1% at the pediatric hematology-oncology center, 81.9% in Pediatric Ward 1 (Department of Infectious Diseases and Pneumo-allergology), 81.9% in pediatric ward 2 (Department of Diabetology, Endocrinology, Neurology, and General Pediatrics), 85.3% in pediatric ward 3 (Department of Gastroenterology, Nutrition, and General Pediatrics), 86.5% in pediatric ward 4 (Department of Cardiology, Nephrology, Rheumatology and Hemodialysis), 84.7% in

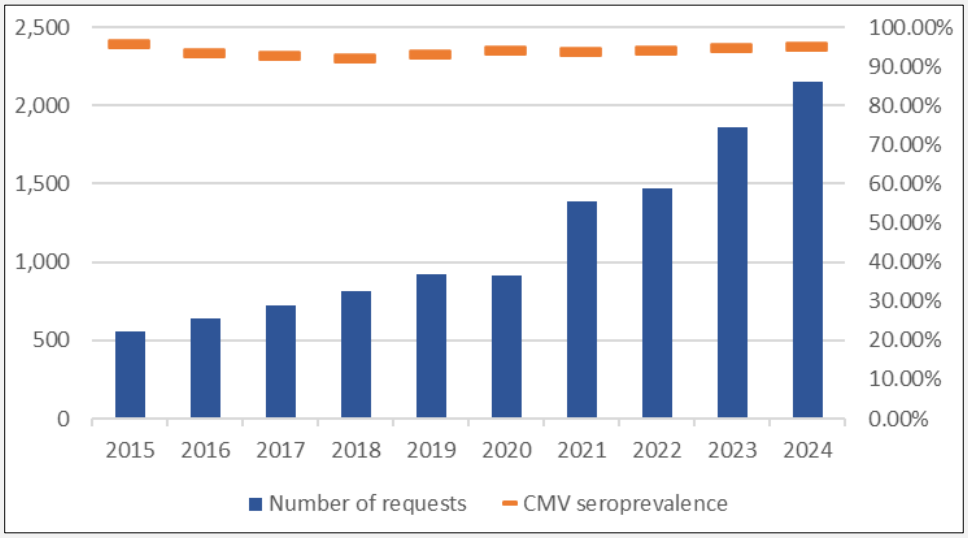

Figure 1. Annual distribution of requests and CMV seroprevalence by year.

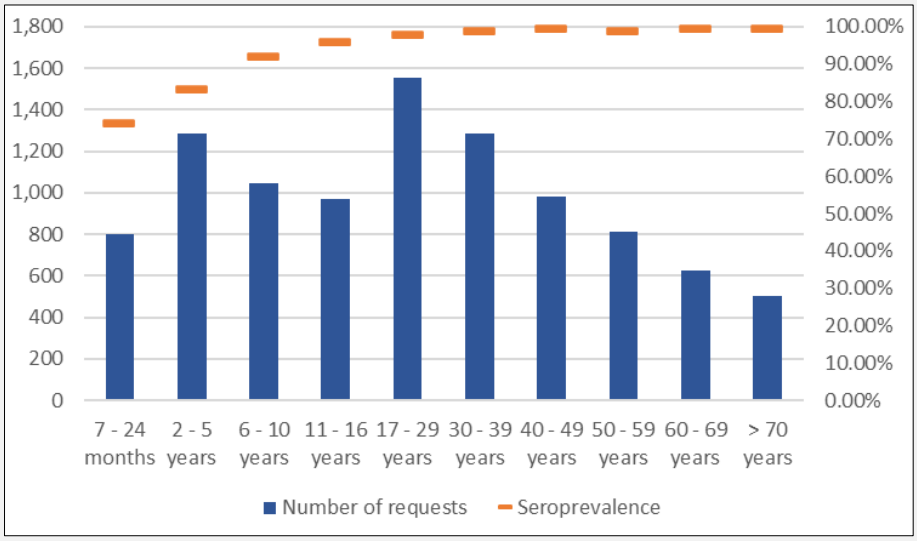

Figure 2. Distribution of requests and CMV seroprevalence by age group.

the Emergency and Intensive Care Unit, and 87.9% among outpatients at the Rabat children hospital.

In this population, seroprevalence increased with age, ranging from 74.0% in infants to 95.6% in adolescents aged 11 - 16 years (Figure 2).

CMV seroprevalence in adults

Among the 7,257 adults included in our study, anti-CMV IgG antibodies were present in 7,145 patients, corresponding to a seroprevalence of 98.5%. No significant difference was observed between males and females ($p = 0.062$). The median age of seropositive pa-

tients was significantly higher than that of seronegative individuals (40 vs. 31 years, respectively; $p < 0.001$).
Seroprevalence rates by department were as follows: 98.9% in the Internal Medicine and Clinical Hematology department, 98.3% in Dermatology, 98.5% in Gynecology, 98.6% in Gastroenterology, 97.4% in Nephrology and Dialysis, and 98.4% in the Emergency and Intensive Care Unit.

DISCUSSION

Our study showed a high overall seroprevalence of CMV in our population, which is consistent with data from the literature. Indeed, in the systematic review and meta-analysis by Mohamed Zuhair et al., the global average CMV seroprevalence was estimated at 83%, with a higher average of 90% reported in countries of the Eastern Mediterranean region [6].
In another systematic review and meta-analysis focused on the blood donor population, which included 43 studies conducted between January 1, 2000, and January 18, 2021, of which 20 were from Africa, 21 from Asia, and 2 from South America, the overall CMV seroprevalence was similarly reported at 83.16% [7].
Several factors appear to influence CMV seroprevalence, including age, gender, ethnicity, socioeconomic status, and number of household members [8-11].
Indeed, seroprevalence varies considerably between countries. In a study conducted in Nigeria in 2010, the CMV seroprevalence among the 192 blood donors included in the study was 95.8% [12]. In another studies, the seroprevalence was reported as 96.4% in Brazil [13], 77.6% in Ghana, and 80.5% in Libya [14]. In contrast, CMV seroprevalence is generally lower in developed countries. In a study conducted in the United States, which analyzed serum samples from the National Health and Nutrition Examination Survey (NHANES) between 1999 and 2004, CMV seroprevalence was found to be 50.4% [11]. These findings were similar to those reported in Germany (56.7 - 57.25%) [10,15], France (41.9%) [16], and the Netherlands (45.6%) [8]. Furthermore, as observed in our study, several other studies have reported an increase in CMV seroprevalence with age [10,15]. Additionally, female gender was associated with higher seroprevalence in several studies, which aligns with our findings [10,15].
Regarding CMV seroprevalence among women, it generally follows the same pattern as in the overall population. It was reported to be 40.9% in Germany [9], 51.5% in France [17], 49% among White British women [18], 66 - 69.1% in Japan [19,20], 71.5% in Finland [21], 72.2 - 97.5% in Sudan [22,23], 88.7% in Southern Ethiopia [24], 96.3% in Tunisia [25], 96 - 97% in Brazil [26,27], and 98.7% in China [28].
The risk of congenital CMV infection exists both in primary maternal infections [5], which occur more frequently in developed countries due to low CMV seroprevalence, and in cases of reactivation or reinfection with a new viral strain, which are more frequent in developing countries such as Morocco.
Among hemodialysis patients, CMV seroprevalence ranged from 27.5% in the study by Michelle Teodoro Alves to 100% in the studies by Lahcen and Aghajanian, according to a systematic review and meta-analysis that included studies conducted between January 1, 2000, and February 1, 2022 [29]. In the Moroccan context, a study conducted on hemodialysis patients in the Nephrology, Dialysis, and Renal Transplantation Department of CHU Ibn Rochd in Casablanca, which included 87 hemodialysis patients and 30 controls, found a seroprevalence of 100% in patients and 96.7% in controls [30]. These findings are consistent with our results.
Moreover, CMV seroprevalence remained stable throughout the study period, which is in line with a study conducted in Korea from January 1995 to December 2015, where no statistical difference was observed between the two studied periods (94.2% (1995 - 2005) vs. 94.1% (2006 - 2015) [31]. However, in a study conducted in Finland, CMV seroprevalence among pregnant women declined from 84.5% to 71.5% between 1992 and 2012 [21].

CONCLUSION

This study showed that CMV seroprevalence in our population is high and aligns with rates observed in other developing countries. In vulnerable populations, particularly women of reproductive age and immunocompromised patients, the risk is mainly related to reactivation or reinfection. Further studies are needed to better analyze the risk of CMV reactivation across different patient profiles in our population and to guide prevention and management strategies.

Data Availability:
The data used to support the results of this study are included within the article.

Source of Funds:
No funding was received for conducting this study.

Declaration of Interest:
The authors declare that there are no conflicts of interest regarding the publication of this article.

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