Research Article ISSN 2639-9458

Microbiology & Infectious Diseases

Seroprevalence and Serological Status of Cytomegalovirus Infection in Patients Received at the Medical Biology Laboratory of Pasteur Institute in Dakar from January 2018 to June 2020

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Received: 17 Sep 2022; **Accepted:** 26 Oct 2022; **Published:** 31 Oct 2022

Citation: Abdou D, Babacar N, Abdoulaye DT, et al. Seroprevalence and Serological Status of Cytomegalovirus Infection in Patients Received at the Medical Biology Laboratory of Pasteur Institute in Dakar from January 2018 to June 2020. Microbiol Infect Dis. 2022; 6(4): 1-4.

ABSTRACT

Background: *Cytomegalovirus (CMV) infection is the most common congenital infection worldwide and remains an important cause of neurological deficits and sensory hearing loss in developed countries. The seroprevalence of CMV infection is age-dependent and correlates with socio-economic level and ethnicity.*

Objective: *To study the seroprevalence and serological status of cytomegalovirus infection in patients received at the laboratory of the Pasteur Institute in Dakar.*

Methodology: *This retrospective study was conducted from January 2018 to June 2020. The determination of anti-CMV antibodies was carried out on the VIDAS 3 automated system (Biomérieux) by ELFA (Enzyme Linked Fluorescent Assay).*

Results: *A total of 418 patients were seen during the study period with a mean age of 30 years and extremes of 2 days and 74 years, the most represented age group was [30-39 years]. The seroprevalence of CMV was 97% with 3 patients presenting anti CMV IgM antibodies (0.7%). For pregnant women, CMV IgG antibodies were found in 139 patients, i.e. a prevalence of 97.3%. Only one pregnant woman was positive for CMV IgM antibody.*

Conclusion: *The high prevalence of CMV infection in the general population shows the problem of this viral pathology, hence the risk of contamination of immunocompromised persons and pregnant women, especially since its screening is not integrated among the routine examinations in our laboratories.*

Keywords
CMV, Antibody, Seroprevalence.

Introduction

Cytomegalovirus (CMV) infection is the most common congenital infection worldwide and remains an important cause of neurological deficit and sensory deafness in developed countries [1,2]. After primary infection, it persists for life in latent form in infected individuals, a potential source of reactivation, which can then lead to new transmissions. Asymptomatic CMV infection in immunocompetent individuals is a source of complications in immunocompromised individuals and is the leading cause of viral congenital infections, for which management strategies vary greatly depending on the country [2]. CMV infections are endemic and occur throughout the year, with no seasonal upsurge. The seroprevalence of CMV infection is age-dependent and correlated with socio-economic level and ethnicity. In countries with a high socio-economic level, the seroprevalence of CMV is

low (< 20%) in children, reaching around 50% in young adults and 80% in the elderly population [3]. Herpes viruses are a real public health problem for pregnant women and newborns, but very little data exists on the prevalence of these viruses in pregnant women in Africa and more particularly in Senegal. It therefore appears essential to take stock of the seroprevalence of CMV infection. Moreover, the ability to reliably identify their primary infection during pregnancy, and thus to integrate possible treatment options for the fetus [4] can reduce the rate of infection and infant mortality. It is important to detect infection with these viruses through an effective diagnostic tool. It is with this in mind that we undertook this study which aims tò investigate the seroprevalence of CMV infections in patients received at the Pasteur Institute of Dakar.

Material and Methods

Study population

All patients who were requested to have CMV serology by their physician during the study period were included in the study.

Sample collection and processing

To carry out the anti-CMV antibody assay (IgM and IgG), venous blood was collected from the elbow using a vacuum sampling system on a dry tube without anticoagulant. The dry tubes were centrifuged at 3000 rpm for 5 minutes. Serum samples could be stored at 2-8°C for up to 5 days or frozen at -25° ± 6 C.

Anti-CMV IgM and IgG antibody assay on VIDAS 3

ELFA procedure

The principle of the assay combines the two-step sandwich enzyme immunoassay with a final fluorescence detection (ELFA) on the VIDAS 3 system. The single-use cone (SPR®) serves as both solid phase and pipetting system. The other reagents of the immunological reaction are ready to use and pre-prepared in the cartridge. All test steps are performed automatically. They consist of a succession of aspiration/refusion cycles of the reaction medium. After an adsorption step for IgG and rheumatoid factor, the sample is aspirated and forced into the cone for a specified time. The anti-CMV IgM antibodies in the sample will bind to the CMV antigen on the inner wall of the cone. Washing steps remove unbound compounds. An alkaline phosphatase labelled anti-human IgM monoclonal antibody is drawn into the cone and binds to the anti-human CMV IgM attached to the cone wall**.** A final wash step removes unbound compounds. In the final development step, the substrate (4-Methyl-ombelliferyl phosphate) is drawn into the cone and the enzyme in the conjugate catalyses the hydrolysis reaction of this substrate to a product (4-Methyl-ombelliferone) whose fluorescence is measured at a wavelength of 450 nm.

Statistical Analysis

Data entry was performed using Excel version 2018 and statistical analysis was performed using Stata 14.0 version 2015.

Results

Socio-demographic characteristics

A total of 418 patients were received at the LBM of the Pasteur Institute of Dakar during the study period for IgM and IgG anti-CMV antibody testing. Women represented 74.9% of the patients, i.e. a sex ratio F/H of 2.9. The mean age was 30 years with extremes of 2 days and 74 years. The most common age group was [30-39 years] (Table 1).

Table 1: Main Socio-Demographic Characteristics.

	Number	%
Sexe		
Women	313	74,9
Men	105	25,1
Sexe ratio H/F	0,33	
Mean age [Extremes]	30 years [2 days – 74 years]	
Age group		
[0-9]	44	10,3
[10-19]	24	5,6
[20-29]	110	25,6
[30-39]	155	36,1
[40-49]	72	16,8
[50-59]	15	3,5
[>=60]	9	2,1
Total	418	100

CMV IgG and IgM antibody results

Serological profile in the population

CMV IgG antibodies were found in 406 patients, i.e. an overall prevalence of 97%, thus indicating contact with the virus in these patients. Among the latter, CMV IgM antibodies were found in only 3 patients (0.7%) (Table 2)**.**

Table 2: Serological Status of CMV Infection in the Population.

Antibodies	CMV IgM (-)	CMV IgM (+)	Total
	N (%)	**N (%)**	**N (%)**
CMV IgG (-) N (%)	12 (3)	0 (0)	12 (3)
CMV IgG (+) N (%)	403 (96,3)	3 (0,7)	406 (97)
Total N (%)	415 (99,3)	3 (0,7)	418 (100)

Distribution of anti-CMV IgG antibodies in pregnant women by age group

The distribution of anti-CMV IgG antibodies in pregnant women by age group shows 100% positivity in the age group >40 years (Table 3).

Table 3: Distribution of Anti-CMV IGG Antibodies in Pregnant Women by Age Group.

Age group	**Number of women**	**Seropositive (%)**	**Seronégative (%)**
21-30	56	54 (96,4)	2 (3,6)
31-40	71	70 (98,6)	1 (1,4)
>40	16	16 (100)	0 (0)
Total	**143**	**140 (98)**	**3 (0,7)**

Serological profile of CMV infection in pregnant women

CMV IgG antibodies were found in 140 pregnant women, i.e. a prevalence of 98% (Table 4). Only one pregnant woman was positive for CMV IgM antibody.

Discussion

During our study, 418 patients were included with a mean age of 30 years and extremes from 2 days to 74 years. These data are

comparable to those reported in Mali and Nigeria with an average age of 30 and 32 years respectively [5,6]. Our study population was dominated by women (74.9%) and the age group [30-39 years] was the most represented (36.1%). This female predominance was found in a study conducted in the USA (60%) [7]. Indeed, female gender was significantly associated with the seroprevalence of cytomegalovirus infection, which could be related to the close contact of women with infants [8], but also by the number of pregnant women included (34%).

Table 4: Serological Status of CMV Infection in Pregnant Women.

ANTIBODIES	CMV IGM (-)	CMV IGM (+)	TOTAL
	N (%)	**N (%)**	**N (%)**
CMV IGG (-) N (%)	3 (2)	0 (0)	3 (2)
CMV IGG (+) N (%)	139 (97,3)	1 (0,7)	140 (98)
TOTAL N (%)	142 (99,3)	1 (0,7)	143 (100)

CMV IgG antibodies were positive in 97% (n=406/418) of our study population, which may reflect previous contact with CMV probably due to promiscuity in developing countries like ours. The high prevalence of CMV IgG antibodies has been reported in studies conducted in Ethiopia in 2014 (98.0%) [9] and Iran in 2013 (98.5) [10]. This high level of CMV IgG antibodies in the population has also been reported in blood donors. Rates of 99.2% and 95.8% were reported in two studies conducted among blood donors in Iran and Edo State, Nigeria, respectively [6,11]. These results had shown the high prevalence of CMV infection in the population according to size, gender or age [12].

The CMV IgM antibody test was positive in 3 patients (0.7%) who also had CMV IgG antibodies, probably as a result of an acute infection or prolonged persistence of IgM or reactivation of the CMV infection. In these 3 patients, avidity testing would have been of interest to date the infection in order to conclude to an acute infection or reactivation. In our study population, pregnant women represented 34% (n=143), hence the interest in determining their immune status with respect to CMV infection. CMV IgG antibodies were present in 98% of pregnant women. In Africa, comparable rates have been reported in Nigeria, 97.2% in 2011 in Lagos State [13] and 91.1% in 2014 Kano State [14]. A comparable rate (98.3%) was reported in 5,959 pregnant women in Izmir, Turkey from 2001 to 2008 [15].

The presence of anti-CMV IgG antibodies in pregnant women could be due to a primary and/or secondary infection with intermittent virus excretion resulting in reactivation of an endogenous virus or exposure to a new strain of virus from exogenous sources. This situation could have consequences for the foetus if the infection occurs in early pregnancy, with neurological sequelae (hearing loss, neurosensory loss, mental retardation etc.).

In pregnant women, the presence of anti CMV IgM antibody was noted in only one individual (0.7%). The retrospective nature of the study did not allow us to know the evolution of the infection in the latter.

The presence of CMV IgM antibody in pregnant women has been reported in Nigeria (4%, 8/200) [16] and Sudan (6%, 12/200) [17].

The variations in CMV infection data reported in the different studies could be explained by the notion of geographical variation [18].

Thus, differences in CMV infection in the general population have been noted worldwide, with rates ranging from 45% to 100%, with higher trends in South America, Africa and Asia, as opposed to Western Europe and the United States where rates are lower. This major disparity in seroprevalence rates by geographical origin could also be related to differences in breastfeeding frequency and duration, childhood hygiene, childcare and sexual behavior [19].

Conclusion

A significant proportion of pregnant women are exposed to CMV infection. We recommend that health policies include routine screening of pregnant women for CMV-Ig or detection of CMV-Ig avidity, mandatory screening of blood for CMV antibodies for transfusion to preterm infants, pregnant women and immunocompromised individuals.

Acknowledgement

Medical biology laboratory of the Pasteur Institute of Dakar (IPD).

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