

Seroprevalence of Cytomegalovirus in Chronic Hemodialysis Patients in Morocco

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Abstract

CMV infection is endemic in most countries of the world. It is likely to take severe forms in immunocompromised individuals hemodialysis patients, given that the seroprevalence is high among the general population. Our study is a prospective description of the seroprevalence of cytomegalovirus among chronic hemodialysis patients in Marrakesh through a serie of 5120 patients treated in the hemodialysis centers of Marrakesh, who's their serum is analyzed in Virology department of the Military Hospital Avicenne, over a period of 64 months, from September 2015 to January 2021. Serological test for the presence of IgG and IgM anti CMV, was performed by immunoassay technique chemiluminescent microparticle (CMIA), by ARCHITECT (ABBOTT DIAGNOSTIC). The prevalence of IgG and IgM anti-CMV was 98% and 0.6% respectively. The mean age of patients with CMV IgG positive was 53 years. The sex ratio was 1.04. Arterial hypertension was present in 52% of CMV positive patients, followed by diabetes (29%). Among our patients, 19% have been on hemodialysis for less than 2 years, while 42% have been treated for 2 to 5 years. 68% of CMV-positive patients are on hemodialysis 3 times a week versus 32% on 2 times. The prevalence of CMV is 63% in transfused patients with an average recurrence of 2 transfusions. Regarding the type of blood transfused, 99.7% of the patients were transfused with standard blood, against 16 patients transfused with leukoreduced blood. We recommend blood transfusion leukodepleted in the hemodialysis population to reduce the risk of transfusion transmission CMV.

Keywords: Seroprevalence - Cytomegalovirus - Chronic hemodialysis patients - IgM antibodies - IgG antibodies - transfusion.

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INTRODUCTION

Chronic renal failure (CRF) corresponds to a progressive and permanent alteration of renal functions. At its terminal stage, periodic hemodialysis represents the first of the palliative treatments of the disease, aiming at prolonging the longevity of uremic patients [1].

However, immunodeficiency during end-stage renal disease (ESRD), recurrent transfusions and the environment of the hemodialysis unit, which is conducive to nosocomial risk, make the hemodialysis population a high-risk group for the acquisition of viral infections, mainly viral hepatitis B (HBV), viral hepatitis C (HCV) and Cytomegalovirus (CMV)[2,3].

CMV is a herpesvirus with vertical, sexual and horizontal transmission. This virus is ubiquitous and endemic worldwide, infecting 50 to 100% of the adult

population [4]. It is also the first cause of congenital viral infection in the world and 0.5 to 1% of newborns are infected at birth.

Although not very pathogenic in the immunocompetent host, CMV is an opportunistic agent responsible for severe clinical manifestations in the immunocompromised [3], particularly in hemodialysis patients [5].

After transplantation, CMV infection most often occurs by reactivation of the virus, and is life-threatening for the recipient [6].

Thus, CMV infection increases the repercussions of the initial disease, generating excess morbidity, excess mortality and significant additional costs. This is why we are witnessing a real deployment of biotechnological forces to fight against this virus that

kills immunocompromised patients in the shadows [7, 8].

The objective of this work is to evaluate the seroprevalence of Cytomegalovirus in a category of patients particularly exposed, chronic hemodialysis patients in the region of Marrakesh.

MATERIALS AND METHODS

This is a retrospective descriptive study on the seroprevalence of Cytomegalovirus in chronic hemodialysis patients in the region of Marrakesh, this over a period of 64 months, from 01/09/2015 to 01/01/2021.

This study was carried out in the Virology laboratory of the Avicenne Military Hospital, in collaboration with eight hemodialysis centers, seven of which are private and one public.

A total of 5120 cases were collected, all of them consenting.

All the records of chronic hemodialysis patients (HD) aged over 16 years, identified during the study period in the centers were analyzed in this study.

Records of patients younger than 16 years, undergoing peritoneal dialysis and patients undergoing occasional hemodialysis were excluded from this study.

The data studied were collected using an operating form combining information from the interview and medical records of chronic hemodialysis patients.

Sociodemographic data concerning age, sex, residential status, and socioeconomic level were specified, as well as clinical data concerning the causative nephropathy, hemodialysis parameters, which are the duration of hemodialysis, the number of dialysis sessions, the vascular approach, and the rhythm of sessions. Recurrence of transfusions, their types, transplant candidates and their viral status, medical-surgical and drug abuse history and clinical symptomatology were analyzed. Biological data such as blood count, liver function tests, and HBV, CVH, and HIV serologies were reported.

The serological analysis was done from 5 ml venous blood samples on sterile tubes with gel separator, dated and identified. The collected whole blood was stored at +4°C and sent immediately to the biology laboratory of the Avicenne military hospital, then centrifuged at 2000 rpm for 15 minutes. The serum was then recovered and aliquoted. A first part was used to perform serological tests and a second part (minimum of 3 aliquots of 500 µl) was frozen for the constitution of a serum library for later analysis.

CMV IgM and IgG antibodies (Ac) were tested by ARCHITECT i1000, a microparticle chemiluminescence immunoassay (CMIA) from its manufacturer ABBOTT DIAGNOSTICS, Reagent Kit, with the following interpretation criteria:

Samples with anti-CMV IgG antibody concentrations: < 6.0 AU/ml (Arbitrary Unit) are considered uninfected for CMV and likely to develop a primary infection.

≥ 6.0AU/ml are considered reactive for these antibodies and indicate past or ongoing infection.

Samples with anti-CMV IgM antibody concentrations: <0.85 index are considered nonreactive for these antibodies and indicate the absence of an acute infection.

≥ 1 index indicate acute infection. Such patients are likely to transmit CMV infection.

These data were entered and coded on SPSS 16.0 software for Windows. Then the resulting data were analyzed by the same software.

The results are expressed as percentages and absolute values for qualitative variables, and as means and extremes for quantitative variables, with the help of graphs or tables.

We collected the data respecting the anonymity of the patients and centers and the confidentiality of their information after agreement.

RESULTS

The overall seroprevalence of CMV was 98% for anti-CMV IgG antibodies and 0.6% for anti-CMV IgM antibodies (Table1).

Table-1: Overall prevalence of anti-CMV IgG and IgM in the study population

	CMV - Ig G	CMV - Ig M
Number	4608	31
Percentage	98%	0.6%

The age of the CMV IgG positive patients in our study ranged from 16 to 92 years with a mean age of 53 years. In our study, advanced age was associated with the high prevalence of CMV in chronic hemodialysis patients.

Our 5120 patients were divided into 2515 women (48.3%) and 2605 men (51.7%) with a sex ratio of 1.04. There was therefore a slight male predominance.

All our patients were from the Marrakesh region with a majority coming from urban areas (78.4%), against 21.6% from rural areas. 54.2% of the

CMV seropositive patients were from a low socio-economic level.

Arterial hypertension was present in 2663 patients, i.e. 52% of CMV positive patients, followed by diabetes which was found in 1485 patients, i.e. 29% of all patients with positive CMV Ig G serology, while 8.3% of the cases studied had no medical history.

Among our patients, 19% have been on hemodialysis for less than 2 years, while 42% have been treated for 2 to 5 years. The prevalence of CMV IgG positive patients does not exceed 18% when this duration is longer than ten years. We illustrated the relationship between the length of time on hemodialysis treatment and the prevalence of previous CMV infection. 68% of CMV-positive patients are on hemodialysis 3 times a week versus 32% on 2 times.

The prevalence of CMV is 63% in transfused patients with an average recurrence of 2 transfusions (Figure 1).

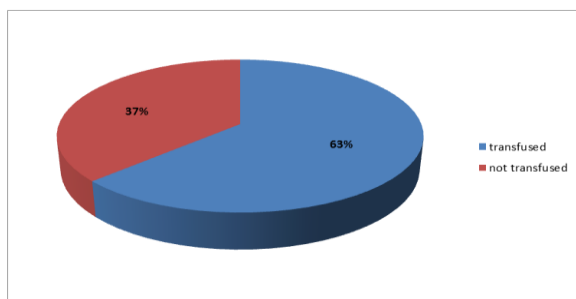


Fig-1: Blood transfusion in CMV + patients.

In our study, 34% of CMV positive patients received 2 red blood cells.

Regarding the type of blood transfused, 99.7% of the patients were transfused with standard blood, against 16 patients transfused with leukoreduced blood.

Among the patients with anti CMV igG, 12% had positive hepatitis C serology, 1% had positive hepatitis B serology and no patient was HIV positive.

DISCUSSION

Our study is certainly one of the first to address this issue in the Moroccan context, which could easily explain a limited literature.

This study, carried out over a period of 64 months, determined the anti CMV serological status (IgG and IgM) of 5120 chronic hemodialyzed patients in the region of Marrakesh, using the chemiluminescence microparticle immunoassay (CMIA).

The prevalence rate of CMV among chronic hemodialysis patients in Marrakesh is 98%, which is in the middle of the literature, where seroprevalence varies between 90 and 100% in developing countries [9].

Thus the level of anti CMV IgG would be in agreement with that reported in Sudan, Egypt, Croatia, Brazil and Iraq [10-18]. In Spain, France, and Australia the prevalence of anti CMV IgG is respectively 62.8%, 41.9% and 59% in the general population, significantly lower than the prevalence in our series [19, 20]. Thus, the prevalence in our study would place our region in a high endemicity area (Table 2).

Table-2: Prevalence of CMV in Chronic Hemodialysis Patients

Autors	Year	Number of cases	Country	Prevalence	
				IgG	IgM
Haitham <i>et al.</i> [10]	2015	93	Sudan	95,7%	45.2%
Awadelkareem <i>et al.</i> [11]	2013	41	Sudan	95%	6%
Abdullah <i>et al.</i> [12]	2011	-	Sudan	98.12%	0%
Ghada <i>et al.</i> [13]	2015	60	Egypt	80%	-
Tamer <i>et al.</i> [14]	2015	99	Egypt	69%	-
Cavlek <i>et al.</i> [15]	2015	162	Croatia	91%	2.5%
Joao <i>et al.</i> [16]	2014	290	Brasil	96%	5.1%
Israa <i>et al.</i> [17]	2015	116	Iraq	87.9%	8.6%
Ansam <i>et al.</i> [18]	2014	91	Iraq	95.6%	-
Our study	2021	5120	Morocco	98%	0.6%

In our study, the mean age of chronic hemodialysis patients positive for CMV type IgG was 53 years. We therefore agree with the results of Cavlek *et al.*, Betjes *et al.*, Kao *et al.*, Ocak *et al.*, Trkulic *et al.*, and Yao-Ming *et al.* who found a significant association between age and CMV IgG seropositivity [15, 2, 21, 22, 23].

This is not the case for the study of Ghada *et al.*, Sepehrvand *et al.*, Ansam *et al.*, Firouzjahi *et al.*, Aminzade *et al.*, and Pliquet *et al.*, who disproved the significant association between anti CMV IgG seropositivity and age [13, 24, 17, 25, 26, 27].

The advanced age of our CMV seropositive patients could be explained by the average age of the

target population itself, which would be in the range of 55-62 years, as there is a tendency for new patients undergoing dialysis to age.

Most series have an equal sex distribution, consistent with the sex ratio noted in our study (1.04). Haitham and Cannon [1, 24, 28] found a male predominance [10, 29].

The length of time on hemodialysis is a very important risk factor for the transmission of cytomegalovirus in chronic hemodialysis patients [30]. In our work, the average duration of hemodialysis in IgG-positive patients was 5.9 ± 5.1 years.

In Morocco, as in most developing countries, systematic screening of labile blood products for cytomegalovirus is not common practice in transfusion centers.

Several studies, notably that of Ansam *et al.*, Abou El Yazed *et al.*, have found that the seroprevalence of CMV is high among hemodialysis patients, and consider that blood transfusion is a major risk factor for CMV contamination [17, 30].

In view of the evidence that leukocytes were the vector of transmission of the infection during transfusions. Leukoreduction was used to reduce the risk of transfusion transmission of CMV. Currently, North America, Europe, Asia and Australia have made this process mandatory for all transfused patients in order to minimize the transmission of leukotropic viruses such as CMV, especially in chronic hemodialysis candidates for transplantation [31].

In Morocco, where the prevalence of CMV reaches 98% both in hemodialysis patients and in the general population, leukodepletion seems to be the best preventive approach to post-transfusion transmission of CMV in immunodeficient subjects. It is a more appropriate and cost-effective alternative in view of the scarcity of blood from seronegative individuals that may be available for transfusion.

CONCLUSION

The seroprevalence of CMV in the hemodialysis population of the Marrakesh region is estimated at 98%; that found in the general population also exceeds 97%.

The very high prevalence of CMV in our environment increases the risk of contamination of immunocompromised persons, especially since its screening is not included in the qualification examinations of blood bags in the different transfusion centers in Morocco.

Post-transfusion transmission of CMV is an important risk factor as long as we use non-leukocyte-

depleted blood. Thus, good safety with respect to the risk of transfusion transmission of CMV requires standardization of leukodepletion.

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