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Seroprevalence of cytomegalovirus antibodies in haemodialysis patients in Morroco

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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 such as allograft recipients of marrow or organ, patients with acquired immunodeficiency syndrome (AIDS) and 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 Marrakech through a serie of 500 patients treated in the hemodialysis centers of Marrakech, whose their serum is analyzed in Virology department of the Military Hospital Avicenne , Marrakech teaching hospital, over a period of 6 months, from September 2015 to March 2016. We collected demographycal, clinical and biological data from the patients records and anamnesis. 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 0.4% respectively. The mean age of patients with CMV IgG positive was 55.95 ± 14.21 years,which 50.2% are from low economic level . The mean hemodialysis duration was 5.9 ± 5.1years among seropositive for CMV IgG, 63.2% of them are undergoing hemodialysis three times a week. 298 (60.3%) patients with IgG anti CMV + were transfused at least once, all by standard blood against 196 (39.7%) patients who have never been transfused. The mean recurrence of blood transfusion is averaging 2.1transfusion.Among anti CMV IgG positive patients, 60.3% had a surgical history against a single patient who has a history of transplantation. Clinically, one patient is symptomatic. 11.9% and 1.4% of CMV seropositive patients have respectively a positive HCV and HVB serology. Anemia was present in 387 (78.3%) of CMV + subjects , while the liver function was normal in most patients. We recommend blood transfusion leukodepleted in the hemodialysis population to reduce the risk of transfusion transmission CMV

INTRODUCTION

Chronic renal failure (CKD) is a progressive and permanent impairment of renal function. In its end stage, periodic hemodialysis represents the first of the palliative treatments of the disease, aimed at prolonging the longevity of uremics [1].

However, immunodeficiency in end-stage renal disease (CRTI), recurrent transfusion and the environment of the hemodialysis unit conducive to nosocomial risk make the hemodialysis

population a high- Viral hepatitis B (HBV), viral hepatitis c (HCV) and cytomegalovirus (CMV) [2, 3].

CMV is a herpesvirus with vertical transmission, sexual but also by contact. This virus is ubiquitous to global endemicity, favored by precariousness: the percentage of adults with anti-CMV antibodies reaches 90 to 100% in developing countries and is less than 50% in developed countries [4].

CMV is a pathogenic agent in the immunocompetent host and is an opportunistic agent responsible for severe clinical manifestations in immunocompromised patients [3], including hemodialysis [5].

In the course of transplantation, CMV infection usually occurs by reactivation of the virus, and involves the functional prognosis of the graft and even vitality of the recipient [6].

Thus, the CMV infection increases the impact of the initial disease, generates an over-morbidity, an excess mortality and a non-negligible surcharge. This is why we are seeing a real deployment of biotechnological forces to fight this virus which kills immunocompromised patients in the shade [7,8].

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

MATERIAL AND METHODS

I. Type of study:

This is a descriptive prospective study of the seroprevalence of Cytomegalovirus in chronic hemodialysis in the Marrakech region over a period of 06 months, from 01/09/2015 to 01/03/2016 .

II. Framework of study:

Study carried out in the laboratory of Virology of the military hospital Avicenne, University Hospital of Marrakech (CHU), in collaboration with five centers of hemodialysis of the private and public sector. 500 cases were collected, all consenting.

The study was carried out in five hemodialysis centers (CH), four of which were private and one public.

III. Inclusion Criteria:

In this study,

• All chronic hemodialysis (HD) cases over the age of 16, identified during the study period in the CH 1, CH 2, CH 3, CH 4, and CH 5 hemodialysis centers .

IV. Exclusion criteria:

Excluded from this study were:

• Records of patients under the age of 16 years.

• Records of patients on peritoneal dialysis.

• Records of patients undergoing hemodialysis on an occasional basis.

• Records identified outside of the study period.

V. Nature and mode of data collection:

The data studied were collected using a data sheet (Appendix I), combining the interrogation information and medical records of chronic hemodialysis patients.

Socio-demographic data on age, sex, residential status, and socio-economic status were specified, along with clinical data on causal nephropathy, hemodialysis parameters such as duration of hemodialysis, Number of dialysis sessions, vascular access and rhythm of sessions. The recurrence of transfusions, their types, candidates for transplantation and their viral status, medical and surgical history and drug addiction and clinical symptomatology were analyzed. Biological data such as blood count, hepatic status, and HBV, HCV and HIV serology have been reported.

-Sample :

The serological analysis was performed from 5 ml venous blood sampling, on sterile tubes with gel separator, dated and identified. The whole blood sample was stored at + 4 ° C and was immediately transported to the biological laboratory of the Avicenna Military Hospital and then centrifuged at 2000 revolutions per minute for 15 minutes. The serum is thus recovered and aliquoted. A first part was used to carry out the serological tests and a second part (minimum of 3 aliquots of 500 µl) was frozen for the constitution of a sero-library for further analysis.

The biological method used is:

Serological test for anti-CMV antibodies (Ac) antibody IgM and IgG by ARCHITECT i1000, a microparticle chemiluminescence immunoassay (CMIA) technique from its manufacturer ABBOTT DIAGNOSTICS, Reagent Kit, whose criteria for interpretation were as follows

Samples with ≥ 1 index concentrations are considered reactive for CMV IgM antibodies and indicate acute infection. Such patients are likely to transmit CMV infection.

VI. Data entry :

This data has been entered and encoded on the SPSS 16.0 software for Windows. Then the data obtained were analyzed by the same software.

The results are expressed as percentages and absolute values for the qualitative, mean and extreme variables for the quantitative variables, using graphs or tables.

VII. Ethical considerations:

We have identified the data by respecting the anonymity of the patients and the centers and the confidentiality of their information after agreement.

RESULTS AND DISCUSSION

1. Epidemiological characteristics:

Our series covers 500 chronic hemodialysis patients collected in the CH1, CH2, CH3, CH4 and CH5 hemodialysis centers, the serum of which has been analyzed at the medical biology department of the Avicenne University Hospital in Marrakech.

Table 1: characteristics of the general population

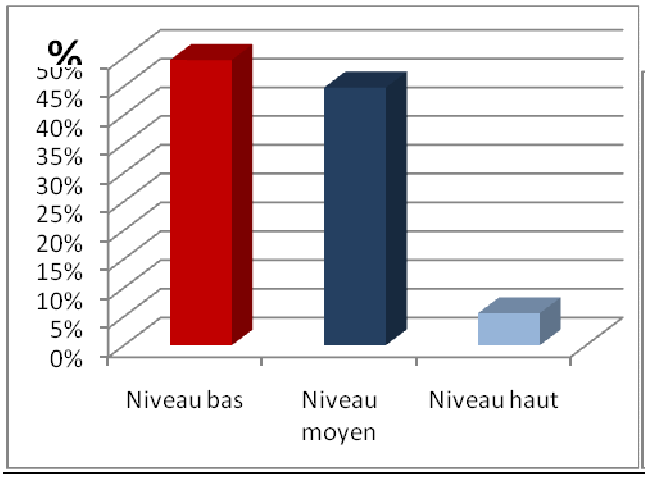
Characteristics	
Number of patients included	500
Average age (year)	55.81±14.31

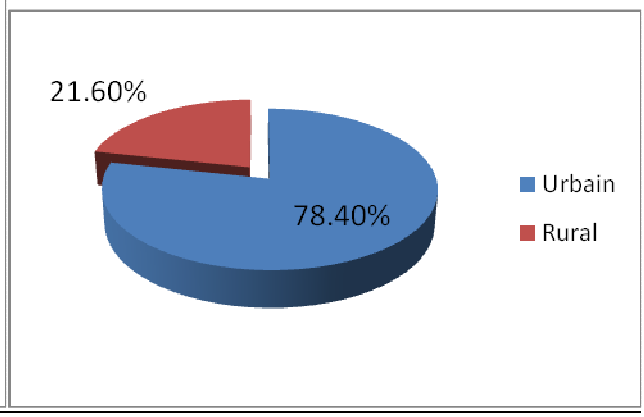
Males (n / a)	255(51%)
Female (n / a)	245(49%)

2. Place of residence and social level of patients

All our patients were from the Marrakech region with a majority coming from urban areas, ie 78.4%, compared with 21.6% of the rural population (Figure 1).

Patients from a low socioeconomic background represent 49.6% of the patients, 44.8% of the patients are of middle medium and 5.6% of the patients are of high socioeconomic level. (Figure 2)





3. Types of nephropathy

Table 2: the different types of nephropathies identified

Type of nephropathy	Number	Percentage (%)
Vascular	120	24
Diabetic	112	22.4
Polycystic kidney disease	26	5.2
Chronic Glomerulonephritis	15	3
Chronic interstitial nephritis	7	1.4
obstructive	3	0.6
Mixed	6	1.2
indeterminate	209	41.8

4. Comorbid history

Table 3: history of comorbidities in hemodialysis patients

History of comorbidities	Number	Percentage (%)
Hypertension (hypertension)	260	52
Diabetes	145	29
heart disease	50	10
Autoimmune disease (AI)	9	1.8
Hepatic Pathology	11	2.2
neoplasia	11	2.2
Cerebral vascular accident (stroke)	7	1.4
Psychiatric follow-up	4	0.8
Chronic respiratory insufficiency	2	0.4
(IRsC)	141	28.2
Nothing to report (RAS)		

5. Overall prevalence of CMV in hemodialysis

Table 4: Overall prevalence of anti-CMV IgG and IgM in the study population

No. of patients	CMV - IgG		CMV-IgM	
	N	%	N	%
	494	98.8	2	0.4

6. Blood transfusion in hemodialysis patients

The prevalence of Cytomegalovirus was 60.3% in transfused patients. However, 196 patients, or 39.7%, were never transfused and yet presented antibodies to CMV +

DISCUSSION

To our knowledge, to date, no Moroccan study has reported the seroprevalence of Cytomegalovirus in chronic hemodialysis in Morocco. This work, carried out over a period of 6 months, made it possible to determine the serological status anti CMV (IgG and IgM) of chronic hemodyalized 500 of the Marrakech region.

Of the 500 chronic hemodialysis patients in our series, 494 patients were seropositive for CMV (anti-IgG positive), which corresponds to an overall prevalence of 98%, indicating prior contact with the virus in this population.

Studies show that 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, by Haitham et al., Awadelkareem et al. And abdullah et al, which was 95.7%, 95% and 98.12% respectively [10,11,12].

Table 5

Authors	School year	Number of cases	Country	Prevalence	
				IgG	**IgM**
Haitham et al. [10	2015	93	Soudan	95,7%	45.2%
Awadelkareem et al. [11]	2013	41	Soudan	95%	6%
Abdullah et al. [12]	2011	_	Soudan	98.12%	0%
Ocack et al. [13]	2006	255	Turquie	99.6%	0.4%
Konstantopoulouet al.[14]	2001	_	Turquie	93%	-
Ghada et al. [15]	2015	60	Egypte	80%	-
Abou El Yazed et al. [16]	2008	100	Egypte	98%	11%
Tamer et al. [17]	2015	99	Egypte	69%	-
Joao et al. [18]	2014	290	Bresil	96%	5.1%
Israa et al. [19]	2015	116	Iraq	87.9%	8.6%
Ansam et al. [20]	2014	91	Iraq	95.6%	-
Aminzadeh et al. [21]	2005	54	Iran	91%	18.8%
Sepehrvand et al. [22]	2010	84	Iran	77.4%	7.1%
Tarabady et al. [23]	2001	_	Iran	100%	-
Betjest et al. [2] [24]	2007	408	Pays-bas	73.8%	-
Cavlek et al. [25]	2015	162	Croatie	91%	2.5%
Cannon et al. [26]	2010	_	Etats Unis	50.4%	_
Trkulic et al. [27]	2000	106	Serbie	99.3%	_
Notre série	2016	500	Maroc	**98%**	**0.4%**

The mean age of chronic hemodialysis with positive anti-CMV IgG ranges from 40 to 66.1 years.

Sepehrvand et al. Found that the mean age of chronic CMV seropositive hemodialysis was 56 ± 16.18 years [22]. In the same sense Ansam et al. Found that 61.53% of HIV-positive patients were in their 40s or 50s [28].

Cavleck et al. Noted that the disease was more frequent in the 50-64 age group with a 49.9% rate, concluding that seroprevalence increases with age [25].

Several authors share the same opinion, Betjes et al., Kao et al., Ocak et al. And Trkulic et al. [2,13,27].

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

Thus, a high prevalence of anti-CMV antibodies in immunosuppressed patients, particularly hemodialysis subjects to repeated transfusions, is due to the transmission of CMV by transfusion [28,29,30,31,32].

In the literature, this finding has been confirmed by numerous studies, particularly in Iraq, where CMV seroprevalence was 79% in hemodialysis patients with a history of blood transfusion.

The American Association of Blood Banks recommends CMV-safe blood transfusion in individuals at risk, which has been adopted in developed countries since the late eighties . These guidelines have helped significantly reduce the transmission of CMV infection in immunocompromised patients [33,34], thus reducing the prevalence of CMV infection [35,36].

In Morocco, leukocyte depletion appears to be the best preventive approach for post-transfusion transmission of CMV in immunocompromised individuals. It is a more appropriate and cost-effective alternative to the scarcity of seronegative blood that may be available for transfusion.

Anemia during CRI is a multifactorial process resulting from the relative deficiency in erythropoietin because uremia induces erythropoiesis inhibitors, decreases the survival of erythrocytes and causes disorders in iron homeostasis [37] . The treatment of anemia in this case would include the administration of iron and erythropoiesis-stimulating agents (ESAs).

Generally young patients receive ESAs, which would decrease the likelihood of transfusion. However, some patients lack of means are transfused [38].

And therefore, standard blood transfusion initiates a vicious cycle of CMV transmission, resulting in seroconversion prompting initiation of antiviral prophylaxis for transplant candidates to combat age-related manifestations , Relating to the change of T cells in immunosuppressive patients.

CONCLUSION

In the hemodialysis population, immunosuppression due to renal insufficiency and the CMV infectious risk incurred during repeated vascular access, make the serological screening necessary in this risk group, in order to avoid the serious damage caused by the possible reactivation Of CMV, to initiate early antiviral therapy, and to identify the serological status of prospective candidates for transplantation.

In order to be able to generalize our results in the Kingdom, similar studies should be conducted at the national level.

The very high prevalence of Cytomegalovirus in our environment increases the risk of contamination of immunocompromised people, especially since its screening is not integrated among the routine examinations in the various blood banks in Morocco.

Post-transfusion transmission of CMV is a major risk factor as long as we use non-leucocyte-depleted blood. Thus, good safety with regard to the risk of transfusion transmission of CMV requires the standardization of leukocyte depletion.

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