

PREVALENCE OF CYTOMEGALOVIRUS INFECTION IN DIFFERENT PATIENT GROUPS OF A URBAN UNIVERSITY IN BRAZIL

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This study sought for evidence of previous CMV infection in patients of a general hospital serving the low income population of Rio de Janeiro. An enzyme immunoassay was used to detect anti-CMV antibodies in 713 typical hospital patients classified into eight different groups. Positive tests were found in 87% of pregnant women, 85% of newborns, 61% of pediatric patients, 77% of adolescent patients, 81% of adult patients, 87% of dialysed transplant candidates, 89% of kidney donors, and 92% of patients after transplantation. Depending of the subgroup studied these results carry different meanings and necessitate different clinical approaches. The risk of congenital disease is probably low in view of the reduced number of pregnant women still susceptible to primary infection. The number of primary infections will also be low in transplant recipients. However, those still susceptible will almost certainly acquire the infection from their donor. Prophylactic CMV matching in kidney transplantation is not a realistic approach due to the low probability of finding pairs of seronegative donors and recipients.

Key-words: Cytomegalovirus. Congenital infection. Immunosuppression. Transplantation.

Most adult individuals display serological evidence of past cytomegalovirus (CMV) infection but the great majority of these episodes are not clinically detected due to their benign nature. After the initial or primary infection, cytomegalovirus usually persists in the host in a latent, non-replicating state. In industrialized countries evidence of past infection is found in 40 to 85% of the adult population³. These figures may vary under geographic and socioeconomic influences so that contact with CMV usually happens at an earlier age and may affect a greater proportion of the population in developing countries¹².

Primary cytomegalovirus infection can be associated with significant morbidity and mortality in certain groups of individuals. Among these are included those with an immature immune system such as fetuses, those with immunodeficiency as a

consequence of disease such as AIDS patients, and those with medically induced immunosuppression such as transplant recipients and cancer patients undergoing therapy⁹.

This study was designed to investigate the prevalence of CMV exposure in patients seen at a tertiary hospital serving the low income urban population of Rio de Janeiro. Our purpose was not to determine the prevalence of CMV infection in the general population. We sought instead to identify rates of exposure to CMV for typical in-hospital patients such as those undergoing medical procedures or treatments that pose a risk of cytomegalovirus transmission or reactivation.

MATERIAL AND METHODS

We surveyed all the tests for CMV serology from SUS (Sistema Unificado de Saúde - Unified Health System) patients submitted to the clinical immunology laboratory of Hospital Universitário Pedro Ernesto between May 1990 and May 1991. A commercial enzyme immunoassay (Abbot CMV Total AB EIA Kit, USA) that detects all classes of immunoglobulins against cytomegalovirus was used throughout the study period. Patients

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with acute illness, already under immunosuppressive therapy (except renal transplant recipients), those with malignant diseases undergoing treatment, and those with confirmed or suspected AIDS were excluded.

We evaluated 713 patients, and classified them into eight different groups according to the source of the specimen: 1) pregnant women, 2) newborns, 3) pediatric patients between 1 and 11 years old, 4) adolescent patients between 11 and 18 years of age, 5) adult patients, 6) renal transplant candidates on dialysis, 7) live kidney donors, and 8) renal transplant patients with more than 6 months after surgery.

Some of the samples were submitted to the laboratory due to a clinical suspicion of CMV infection. It is possible that this procedure biased the study through the inclusion of patients with active infection. This selection bias was partially dealt with by only recording the first serum sample for each individual patient. Presumably these samples were taken at a time when seroconversion had not happened yet and, therefore, represent the prevalence for that particular group.

The prevalence rates between groups of interest were compared using the chi-square test. Significance was set at $p \leq 0.05$.

RESULTS

We were able to collect samples from 54 pregnant patients and their offspring (one twin pregnancy). We also collected 40 additional samples from newborns transferred to our hospital and that had routine determination of CMV serology. Results for the group of paired mothers and newborns showed an almost exact correspondence (87.0% vs 83.6%) except for two newborns with absorbance reading in the undetermined zone (Table 1). The 40 other newborns also showed similar prevalence rates (87.5%). All these results are not significantly different from each other ($p > 0.05$).

Table 1 - Pregnant mothers and newborns with positive cytomegalovirus serology.

Patient groups	Nº tested	Nº positive	%*
Pregnant women	54	47	87,0
Offspring **	55	46	83,6
Transferred newborns	40	35	87,5
All newborns	95	81	85,2

* $p > 0.05$ for all groups

** one twin pregnancy.

Table 2 shows the results for three groups stratified by age. Prevalence rates increased according to the age strata the patient belonged to. They show a trend for acquisition of infection early in life. The rates however are significantly different only for pediatric patients in relation to the adult group ($p < 0.001$).

Table 2 - Hospital patients with positive cytomegalovirus serology.

Patient groups	Nº tested	Nº positive	%
Pediatric patients	118	72	61,0
Adolescent patients	39	30	76,9
Adult patients	121	98	81,0*

* $p < 0.05$ - adult vs pediatric patients.

Results for transplant patients and donors are depicted on Table 3. All three groups show higher prevalence rates than the group of general adult in-patients. However, when compared to those adult patients, the rates are significantly different only for patients which have undergone transplantation ($p < 0.05$).

Table 3 - Transplant patients and donors with evidence of previous cytomegalovirus infection.

Patient groups	No. tested	No. positive	%*
Kidney donors	75	67	89,3
Renal transplant candidates	146	127	87,0
Renal transplant recipients	65	60	92,3

* $p > 0.05$ for all groups.

DISCUSSION

Cytomegalic inclusion disease of the newborn is almost always the result of transplacental transmission during primary infection of the mother⁸. Children of mothers with reactivated CMV infection may acquire the virus but these episodes do not usually result in significant disease⁸. Therefore, knowledge about the rates of pregnant women still susceptible to primary infections in a given population are informative of the risk of CMV disease to their offspring. The lesser these rates are, the lower is the risk of CMV inclusion disease developing in the newborn⁹.

Our study, as well as previous studies in São Paulo and Rio de Janeiro^{4,7}, have documented high rates of positive CMV serology in newborns suggesting that this was due to passive transfer of maternal IgG antibodies. Since we tested samples from pairs of pregnant women and their newborn children, the concordant results is in agreement with this proposition.

For methodological reasons, we were not able to ascertain the exact age of the patients. Our results therefore must be taken with certain caution. Particularly in children's group (less than 11 years of age) the rates of patients with positive serology is expected to change dramatically early in life. Nevertheless, the data does serve to demonstrate that the individuals in the hospital population under study did acquire the infection early in life, displaying a high prevalence of past-contact with CMV. This pattern is characteristic of low income populations in developing countries^{7,12}.

Our figures for adult patients and for organ donors are somewhat lower than in another study of CMV serology done on first time blood donors in the city of Rio de Janeiro. That report found a 97% prevalence rate of anti-CMV antibodies¹⁴. This discrepancy may perhaps be ascribed to the different methodologies used in the two studies. However, 31% of those same blood donors also had serological evidence of contact with the hepatitis B virus¹⁴, suggesting that they were somehow selected to include high risk individuals.

The situation for organ (and blood) donors and their recipients is, in relation to the risk of developing clinically significant disease, diametrically opposite to that of pregnant mothers and their offspring. The viral multiplication of active infection is not a prerequisite to viral transmission. Latently infected transfused or transplanted cells can convey the virus should a non-infected susceptible individual receive them³. These infections can evolve with a very severe clinical course, particularly in patients with immunological deficiency or immaturity³. In immunosuppressed patients, the number of individuals at risk of developing aggressive primary infections is lower in populations with a high prevalence of seropositives. However, in those that are still susceptible, the risk of developing the disease rises with the prevalence of past-contact with CMV in the donor population.

We and other workers in Brazil have previously found lower rates of positive CMV serology in prospective kidney recipients^{6,11}. This was probably due to the less sensitive assays used at that time. The current results show that only 13% transplant candidates are still susceptible to primary CMV infection. As

expected, kidney donors also had a very high prevalence of positive CMV serology. As a consequence, the few susceptible seronegative transplant recipients will have a 9 in 10 chance of being exposed to CMV carried within the graft. Probably for this reason, post-renal transplant patients showed higher seroprevalence rates than other groups of individuals.

One last point that deserves comment is the recent proposition of allocating kidneys of CMV seronegative donors to CMV seronegative recipients (CMV matching) in order to prevent the occurrence of the more severe primary infections¹³. Our results suggest that this approach may not be practical to implement. From the data presented, one can infer that the probability of matching CMV seronegative kidney donors and recipients is under 1.4%. Since, this will be done in addition to the more important immunological compatibility matching, this procedure will almost certainly severely reduce the chances of transplantation for CMV seronegative recipients. Other strategies such as immunization¹ or drug prophylaxis² will probably be more practical and effective for preventing CMV disease in seronegative kidney recipients¹⁰.

In conclusion, the population in the general hospital studied showed high rates of previous contact with CMV. These figures carry different meanings and necessitate different clinical approaches depending of the subgroup of patients the hospital physician is caring for.

RESUMO

Evidência de infecção passada por citomegalovírus foi pesquisada em pacientes de um hospital que serve à população de baixa renda na cidade do Rio de Janeiro. Realizou-se, com um imunoensaio enzimático, a pesquisa de anticorpos anti-CMV em 713 pacientes hospitalares, divididos em oito grupos. As taxas observadas foram 87% para grávidas, 85% para recém-natos, 61% para pacientes pediátricos, 77% para adolescentes e 81% para adultos, 87% para pacientes em diálise, 89% para doadores de rim e 92% para pacientes após o transplante renal. Estes resultados têm diferentes significados e implicam em diferentes abordagens clínicas dependendo do subgrupo estudado. O risco de infecção congênita provavelmente é baixo devido ao reduzido número de mulheres grávidas ainda suscetíveis a infecções primárias. Pelo mesmo motivo, o número de infecções primárias deverá ser

baixo nos transplantados renais. Entretanto, os soronegativos quase certamente adquirirão a infecção de seu doador e a compatibilização de doadores e receptores soronegativos não deverá ser uma abordagem realística devido à baixa probabilidade de encontrar este tipo de par.

Palavras-chaves: Citomegalovírus. Infecção congênita. Imunosupressão. Transplante.

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