

*Full Length Research Paper*

## **Seroprevalence of cytomegalovirus in solid organ donors from Ceará (Brazil), 1998-2010**

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### **Abstract**

**Cytomegalovirus (CMV) infection is an important cause of morbidity in solid organ transplantation. To determine the seroprevalence of CMV in solid organ donors from Ceará, Brazil, and estimate the actual risk of a CMV-negative patient receiving an organ from a CMV-positive donor. Cross-sectional, retrospective study based on active search of notification forms of 660 effective organ donors registered with the Ceará Transplantation Center between 1998 and 2010. With an average age of 33.8±15 years (range: 1.5-70), donors were predominantly male (69.2%). The overall seroprevalence of anti-CMV IgG antibodies was 81.2%, with no significant difference between the genders. On the average, CMV-positive male donors were younger than female donors (33.3 ± 0.75 vs. 37.6 ± 1.16 years) ( $p=0.0017$ ). The prevalence of CMV was slightly lower in 2001 (68.4%), 2002 (65%) and 2010 (74.4%). In all other years, the prevalence was above 78%. CMV positivity was 80.8% for kidneys, 82% for livers and 80.9% for hearts of a total of 1241 grafts transplanted. The prevalence of seropositivity for CMV was high and relatively stable in solid organs donors from Ceará over the past 13 years, suggesting the need to obtain informed consent from CMV-negative solid organ recipients and to develop strategies to prevent primary CMV infection or reactivation in the post-transplantation period.**

**Keywords:** Cytomegalovirus, solid organ transplantation, seroprevalence, donation of organs.

## **INTRODUCTION**

Cytomegalovirus (CMV) infection is an important cause of morbidity in solid organ transplantation, with an incidence of 20-60% and mortality rates up to 90% (Opelz et al., 2004). In addition to direct morbidity, CMV is associated with immunosuppression and, consequently, increased risk of opportunistic infection and graft dysfunction (Dropulic, 2006).

The epidemiology of CMV is region-specific (Sinclair and Sissons, 2006). In general, the seroprevalence of CMV is 40-60% in the northern hemisphere and 80-100%

in Africa and Latin America (Kothari et al., 2002). So far, no study has specifically determined the prevalence of CMV in the Brazilian population as a whole, but rates between 65% and 85% have been observed for particular age ranges and population groups (Suassuna et al., 1995; Biasoli, 1998).

CMV acts like a latent infection which may be reactivated in patients with lowered immunity, such as solid organ recipients treated with immunosuppressant (Sinclair and Sissons, 2006). Thus, transplantation of organs from CMV-positive donors can result in primary CMV infection, or subsequent reactivation, in immunosuppressed individuals (Delmonico, 2000). The main risk factor associated with the occurrence of primary

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CMV infection in the post-transplantation period is the serological profile of donor and recipient (Humar et al., 2004). CMV-negative organ recipients receiving organs from CMV-positive donors are at high risk of primary infection. Thus, active symptomatic disease occurs in approximately 80% of liver transplantations and in 60% of kidney transplantations (Fishman and Rubin, 1998; Guirado et al., 2008).

Anti-CMV IgG antibody tests are routinely used to assess potential cadaver donors, but CMV positivity is not a contraindication for donation (Humar et al., 2004). The purpose of the present study was to determine the seroprevalence of CMV in solid organ donors from Ceará, Brazil, and estimate the actual risk of a CMV-negative patient receiving an organ from a CMV-positive donor.

## MATERIALS AND METHODS

Cross-sectional and retrospective, the study was based on a review of secondary data retrieved through an active search of notification forms of 660 effective organ donors registered with the Ceará Transplantation Center (Northeastern Brazil) between 1998 and 2010. The study was previously approved by the Research Ethics Committee of the University of Fortaleza (UNIFOR) under entry #003/2009.

Demographic and laboratory data for cadaver donors covered gender, age, year of donation, type of solid organ donated (kidney/liver/heart) and result of serology for anti-CMV IgG antibodies. The donors were distributed by age into seven groups at 10-year intervals (the last being 60 years and up). Donors with incomplete information and donors from other Brazilian states were excluded from the sample.

The sera of the cadaver donors were tested at the Central Laboratory of the Ceará State Health Department (LACEN) for the presence of anti-CMV IgG antibodies by microparticle enzyme immunoassay (MEIA) (Abbott®), following the instructions of the manufacturer.

The collected data were organized with Microsoft Excel 2010, with qualitative data expressed as frequency and quantitative data expressed as mean  $\pm$  standard deviation. Using the software GraphPad Prism, the data were submitted the chi-square test and ANOVA, followed by the Student-Newman Keuls test. The level of statistical significance was set at  $p < 0.05$ .

## RESULTS

The sample consisted of 660 solid organ donors from Ceará aged  $33.8 \pm 15$  years on the average (range: 1.5-70), 457 of whom were male (69.2%). The average age was lower for men ( $32.5 \pm 0.7$  years) than for women ( $36.8 \pm 1.1$  years) ( $p = 0.0006$ ).

Anti-CMV IgG antibodies were detected in the sera of 536 donors (81.2%). Seropositivity for CMV was more prevalent among women (84.7% vs. 79.6%), though not significantly ( $p = 0.12$ ). On the average, male donors were younger than female donors, whether CMV-positive ( $33.3 \pm 0.75$  vs.  $37.6 \pm 1.16$  years) or CMV-negative ( $29.3 \pm 1.5$  vs.  $32.4 \pm 3.1$  years), but the difference was only significant in the former group ( $p = 0.0017$ ).

Figure 1 shows the distribution of 536 CMV-positive donors from Ceará in the period 1998-2010. The prevalence of CMV was slightly lower in 2001 (68.4%), 2002 (65%) and 2010 (74.4%). In all other years, the prevalence was above 78%.

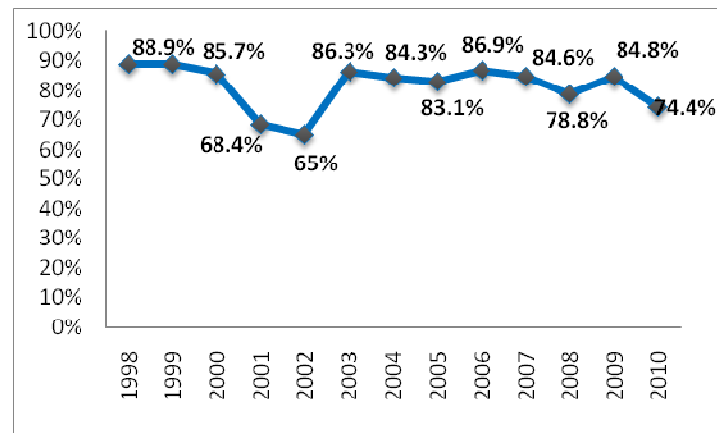
As shown in Figure 2, seropositivity for CMV was most prevalent in the age range 40-49 years (87.2%), followed by the ranges 50-59 years (86.4%),  $\geq 60$  years (85.3%) and 20-29 years (83.3%). Table 1 shows the results of the serology for CMV of all 660 donors in the sample according to gender and age range. The age groups did not vary significantly with regard to gender-related differences in seropositivity.

Between 1998 and 2010, 1241 solid organs from 660 cadaver donors were transplanted in Ceará, including 526 (42.4%) kidneys, 516 (41.6%) livers and 199 (16%) hearts. Of these, 425 (80.8%) kidneys, 423 (82%) livers and 161 (80.9%) hearts were donated by CMV-positive donors (Figure 3).

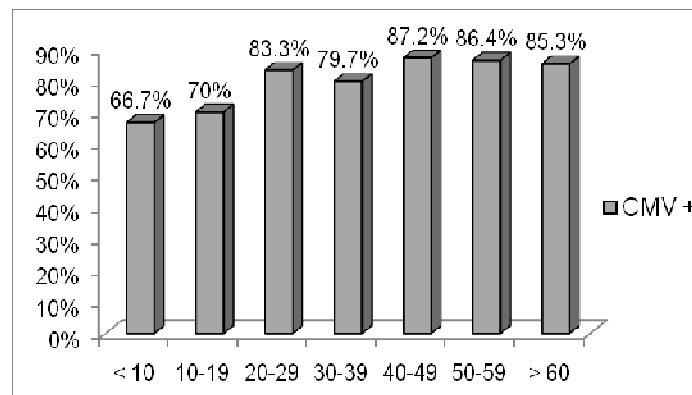
## DISCUSSION

This is to our knowledge the first study in Northeastern Brazil evaluating the prevalence of seropositivity for CMV in solid organ donors. Our findings revealed a high prevalence (81.2%) of seropositivity for CMV over the past 13 years. According to Suassuna and coworkers (1995), seroprevalence rates for CMV vary between populations and age groups, and is inversely proportional to socioeconomic level (Suassuna et al., 1995; Sinclair and Sissons, 2006). A study from Rio de Janeiro (Southeastern Brazil) found that 87% pregnant women, 85% neonates, 61% children, 77% adolescents, 81% adults, 87% dialysis patients and 92% graft recipients at a university hospital were CMV-positive (Suassuna et al., 1995). In two other Brazilian studies on blood donors, seroprevalence was 87.9% (Bahia, northeastern region) and 96.4% (Santa Catarina, southern region) (Matos et al., 2010; Souza and Passos, 2010).

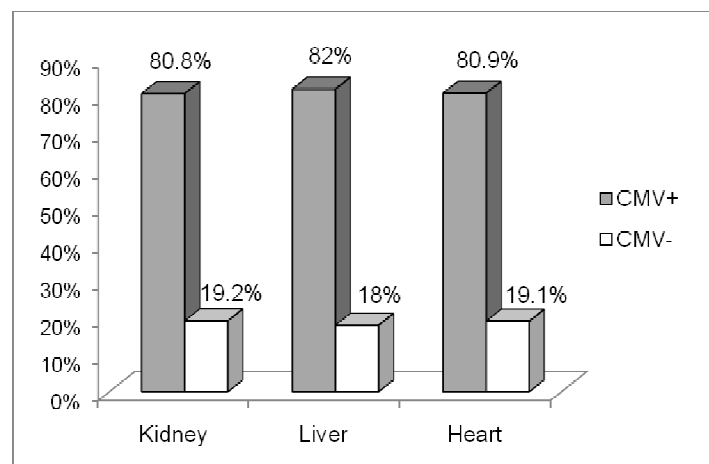
In view of the scarcity of organs for transplantation, the use of grafts from CMV-positive donors (Ceará 81.2%, Santa Catarina 90.7%, Rio de Janeiro 89%) is not contraindicated (Suassuna et al., 1995; Amaral et al., 2008). However, the serological profile of both donor and recipient should be investigated prior to transplantation to assess the actual risk of transmission and primary CMV infection in seronegative recipients and decide on prophylactic or preemptive measures, as the case may



**Figure 1.** Distribution of 536 cytomegalovirus-positive solid organ cadaver donors according to year of donation. Ceará, Brazil, 2008-2010.



**Figure 2.** Distribution of 536 cytomegalovirus-positive (CMV+) solid organ cadaver donors according to age range. Ceará, Brazil, 2008-2010.



**Figure 3.** Distribution of types of organs obtained from cadaver donors according to result of serology for cytomegalovirus (CMV). Ceará, Brazil, 2008-2010.

**Table 1.** Distribution of 660 solid organ cadaver donors according to age range, gender and result of serology for cytomegalovirus (CMV). Ceará, Brazil, 2008-2010.

Age range (years)	Male			Female		
	CMV+	CMV-	Total	CMV+	CMV-	Total
<10	8 (61.5%)	5 (38.5%)	13	6 (75%)	2 (25%)	8
10 - 19	52 (69.3%)	23 (30.7%)	75	18 (72%)	7 (28%)	25
20 - 29	114 (82.6%)	24 (17.4%)	138	31 (86.1%)	5 (13.9%)	36
30 - 39	76 (79.2%)	20 (20.8%)	96	30 (81.1%)	7 (18.9%)	37
40 - 49	56 (83.6%)	11 (16.4%)	67	46 (92%)	4 (18%)	50
50 - 59	39 (84.8%)	7 (15.2%)	46	31 (88.6%)	4 (11.4%)	35
≥ 60	19 (86.4%)	3 (13.6%)	22	10 (83.3%)	2 (16.7%)	12
TOTAL	364 (79.6%)	93 (20.4%)	457	172 (84.7%)	31 (15.3%)	203

be (Opelz et al., 2004; Humar et al., 2004). It has been estimated that, within one year of transplantation, 75% of CMV-negative patients receiving grafts from CMV-positive donors are likely to develop active CMV infection followed by rejection with or without graft loss or death, stressing the importance of CMV infection as a cause of morbidity and mortality in transplantation patients (Fishman and Rubin, 1998; Rubin, 1999; Delmonico, 2000; Humar et al., 2004;).

Our findings match those of previous studies showing that iatrogenesis, by way of organ transplantation, is the main route of transmission of primary CMV infection in CMV-negative graft recipients, as over 80% of the transplantations in Ceará over the past 13 years were performed with grafts from CMV-positive donors (Ho et al., 1975). The number of CMV-negative patients submitted to transplantation in this period is not known, but in a study conducted in 2005 the authors found 42% of the transplantation patients awaiting kidney transplantation in Ceará to be CMV-negative (Silva et al., 2005). Thus, if we consider the number of kidney transplantations performed between 1998 and 2010 with grafts from CMV-positive donors (425/526; 80.8%), the chance of a CMV-negative patient receiving a graft from a CMV-negative donor (19.2% of donors in the study period) is rather small.

In view of these findings, we suggest CMV-negative transplantation patients be informed during pre-transplantation treatment about the risk of receiving a graft from a CMV-positive donor. The decision of whether to accept a graft under these circumstances should be taken jointly by the physician, the patient and the patient's family at this time, rather than at the time of transplantation.

In this study, gender-related differences in seroprevalence for CMV were not significant ( $p=0.12$ ), but Amaral and coworkers (2008) observed a higher prevalence among male organ donors from Santa Catarina ( $p=0.04$ ) (Amaral et al., 2008). On the other hand, studies on blood donors from Bahia and Santa Catarina yielded conflicting results: the prevalence was greater among men in the former, and among women in the latter (Matos et al., 2010; Souza and Passos, 2010).

Lopo and colleagues (2011) believe the higher rates of seroprevalence among women may be explained by their greater vulnerability to horizontal transmission, since mothers, pregnant women and female caretakers (such as teachers and babysitters) are at increased risk of acquiring CMV infection (Lopo et al., 2011).

## CONCLUSION

Over the past 13 years solid organ donors from Ceará have displayed a high and relatively stable prevalence of seropositivity for CMV. Our findings suggest the need to obtain informed consent from CMV-negative solid organ recipients and to better define prophylactic and preemptive strategies to prevent primary CMV infection or reactivation in the post-transplantation period.

## REFERENCES

- Amaral RP, Saidneuy AE, Ribeiro WL, Andrade J (2008). Serological profile of potential solid organ donors in Santa Catarina, Brazil. *Transplant Proc.* 40:665-667.
- Biasoli R (1998). Pesquisa de soropositividade para CMV através de anticorpos totais IgG e IgM em doadores em potencial de plaquetas para TMO alogênico. *Rev Bras Hematol Hemoter.* 20:57.
- Delmonico LF (2000). Cadaver donor screening for infectious agents in solid organ transplantation. *Clin. Infect. Dis.* 31:781-786.
- Dropulic LK (2006). The impact of cytomegalovirus infection on solid organ transplantation. *Adv. Stud. Med.* 6:319-328.
- Fishman JA, Rubin RH (1998). Infection in organ-transplant recipients. *N. Engl. J. Med.* 338:1741-1751.
- Guirado LL, Rabella N, Díaz JM, Facundo C, Maderuelo A, Margall N, Silva I, Garcia-Maset R, Calabia J, Gimenes I, Garra N, Sola R, Ballarín JA (2008). Tratamiento profiláctico y anticipado de la infección por citomegalovirus en pacientes trasplantados renales mediante valganciclovir oral. *Nefrología.* 28:293-300.
- Ho M, Suwansirikul S, Dowling JN, Youngblood LA, Armstrong JA (1975). The transplanted kidney as a source of cytomegalovirus infection. *N. Engl. J. Med.* 293:1109-1112.
- Humar A, Paya C, Pescovitz MD, Dominguez E, Washburn K, Blumberg E, Alexander B, Freeman R, Heaton N, Mueller B (2004). Clinical utility of cytomegalovirus viral load testing for predicting CMV disease in D+/R- solid organ transplant recipients. *Am. J. Transp.* 4:644-649.
- Kothari A, Ramachandran VG, Gupta P, Singh B, Talwar V (2002). Seroprevalence of cytomegalovirus among voluntary blood donors

- in Delhi, India. *J. Health Popul. Nutr.* 20:348-351.
- Lopo S, Vinagre E, Palminha P, Paixão MT, Nogueira P, Freitas MG (2011). Seroprevalence to cytomegalovirus in the portuguese population, 2002-2003. *Eurosurveillance.* 16:1-6.
- Matos SB, Meyer R, Lima FWM (2010). Seroprevalence of cytomegalovirus infection among healthy blood donors in Bahia State, Brazil. *Rev Bras Hematol. Hemoter.* 32:45-49.
- Opelz G, Dohler B, Ruhenstroth A (2004). Cytomegalovirus prophylaxis and graft outcome in solid organ transplantation: A collaborative transplant study report. *Am. J. Transplant.* 4:928-936.
- Rubin RH (1999). Importance of CMV in the transplant population. *Transplant Infect. Dis.* 1:3-7.
- Silva SL, Silva SFR, Oliveira CMC, Nato JSG, Ribeiro IF, Almeida ERB, Esmeraldo RM (2005). Receptor renal CMV negativo deve aguardar um doador cadáver CMV negativo? In: IX Congresso Brasileiro de Transplantes de Órgãos e Tecidos, Salvador. Abstract published in the book of the Brazilian Congress. Pp. 168.
- Sinclair J, Sissons P (2006). Latency and reactivation of human cytomegalovirus. *J. Gen. Virol.* 87:1763-1779.
- Souza MA, Passos AM, Treitinger A, Spada C (2010). Seroprevalence of cytomegalovirus antibodies in blood donors in Southern, Brazil. *Rev. Soc. Bras. Med. Trop.* 43:359-361.
- Suassuna JH, Leite LL, Villela LH (1995). Prevalence of cytomegalovirus infection in different patient groups of an urban university in Brazil. *Rev. Soc. Bras. Med. Trop.* 28:105-108.