



# Infecções Emergentes em Tranplantes de Órgãos Sólidos

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# Introdução

- Infecção é o principal evento adverso pós transplante
- A ocorrência de infecção pode determinar a redução da sobrevida do enxerto e morte.
- Desde o período de pós-operatório precoce as infecções bacterianas podem estar presentes.

**Table 1. Rare and Emerging Viral Infections in the Transplant Population: Case Series or Multiple Cases Reported**

Virus	Virus Family	Transplant	Clinical Manifestations	Comments
HTLV-1	<i>Retroviridae</i>	SOT and HSCT; donor-derived infections reported	Adult T-cell leukemia and HTLV-1-associated myelopathy	Associated with lower survival after HSCT from HTLV-1+ donor
HEV	<i>Hepeviridae</i>	SOT predominantly; case report in HSCT	Chronic viremia, elevated LFTs, cirrhosis; rare reports of neurological complications	Typically de novo infections; treatment possible with reduced immunosuppression, peg-interferon, or ribavirin
Rabies	<i>Rhabdoviridae</i>	SOT, ileac artery graft, cornea transplants; all cases donor derived	Fatal encephalitis; cornea transplants present with pain in eye with graft	Survivors reported cornea transplant with immediate PEP; liver transplant 20 y after vaccination
LCMV and novel arenavirus	<i>Arenaviridae</i>	SOT; all reported cases donor derived	Fever, abdominal pain, nausea, vomiting, diarrhea, altered mental status; often peri-incisional rash and tenderness	14 of 17 patients died; ribavirin employed but effect unclear; 3 cornea transplants unaffected
Measles	<i>Paramyxoviridae</i>	SOT and HSCT	Occasional clinical measles; SME (afebrile, altered mental status, intractable seizures); interstitial pneumonia	SME fatal in 4 of 6 transplant patients; case series suggest severe measles represents minority of cases in transplant recipients
Mumps	<i>Paramyxoviridae</i>	SOT and HSCT	Parotitis, orchitis, vestibular neuronitis, and renal allograft involvement (SOT); fatal encephalitis (HSCT)	3 cases in SOT, all renal transplant patients and all survived; 2 encephalitis cases peri- and post-HSCT
Dengue	<i>Flaviviridae</i>	SOT and HSCT	Dengue fever; severe dengue, including hemorrhagic fever and shock	Dengue shock associated with high mortality; rates of severe dengue differ in case series
Orf	<i>Poxviridae</i>	SOT; contact with infected sheep	Giant and recurrent skin lesions on hands and forearms	Often misdiagnosed and treated with excision or amputation; case reports document responses to cryotherapy, cidofovir cream, or imiquimod
HCoV-HKU1 and -NL63	<i>Coronaviridae</i>	SOT and HSCT	Cases of fatal LRTI, predominantly in SOT; increased risk of lung transplant rejection	Novel beta HCoV identified in 2012 with high rate of fatalities; no reported cases in transplant

Abbreviations: HCoV-HKU1, human coronavirus HKU1; HEV, hepatitis E virus; HSCT, hematopoietic stem cell transplantation; HTLV-1, human T-cell leukemia virus type 1; LCMV, lymphocytic choriomeningitis virus; LFTs, liver function tests; LRTI, lower-respiratory-tract infection; NL63, human coronavirus NL63; PEP, postexposure prophylaxis; SME, subacute measles encephalitis; SOT, solid organ transplant.

## Rare and Emerging Viral Infections in Transplant Recipients

# Hepatite E em transplante

- 14 pacientes tx rim ou rim-pâncreas
- 8 evoluíram com hepatite crônica
- 5 casos de glomerulonefrite associada ao vírus

(Transplantation 2012;93: 617–623)

N Engl J Med 2008;358:811-7.

# Primeiros casos publicados

Tx renal

96 amostras guardadas de 98 a 2007

TABLE I. Characteristics of Transplant Patients at HEV RNA Identification

Case	Year	Age	Gender	Months since transplantation	Donor	Immunosuppressive therapy
1	2002	53	Male	13	Living	Sirolimus/Cyclosporin A
2	2006	27	Male	6	Cadaveric	Azathioprine
3	2007	26	Female	60	Cadaveric	Sirolimus

Passos AM. **Journal of Medical Virology** 85:615–619 (2013)

# Past and Current Hepatitis E Virus Infection in Renal Transplant Patients

Tiago Hering,<sup>1</sup> Ana Maria Passos,<sup>2</sup> Renata Mello Perez,<sup>3</sup> Juliana Bilar,<sup>1</sup> Daniel Fragano,<sup>1</sup> Celso Granato,<sup>2</sup> José Osmar Medina-Pestana,<sup>4</sup> and Maria Lucia Gomes Ferraz<sup>1\*</sup>

Tx renal 2001-2011

TABLE II. Prevalence of HEV Markers in the Three Groups Studied

	Group 1 (n = 61)	Group 2 (n = 37)	Group 3(n = 94)	P-value
Anti-HEV IgG	3 (5%) <sup>a</sup>	10 (27%)	15 (16%)	0.009
HEV RNA	7 (12%)	5 (14%)	8 (9%)	0.6
Anti-HEV and/or HEV RNA	10 (16%) <sup>b</sup>	13 (35%)	21 (22%)	0.1

Group 1: HBV or HCV; group 2: liver disease; group 3: no liver disease, no infection with HBV or HCV.

<sup>a</sup>Group 1 versus group 2 ( $P = 0.004$ ); group 1 versus group 3 ( $P = 0.036$ ); group 2 versus group 3 ( $P = 0.147$ ).

<sup>b</sup>Group 1 versus group 2 ( $P = 0.034$ ); group 1 versus group 3 ( $P = 0.366$ ); group 2 versus group 3 ( $P = 0.13$ ).

# Vírus Respiratórios

**Viral distribution, viral shedding, and symptoms presented by transplant patients with acute respiratory illness in Southern Brazil, over a 1-year period (2011–2012)**

Patients	Virus	Symptoms	Viral shedding (days)
1	hMPV	Fever, myalgia, runny nose, and cough	0
2	RSV	Fever and cough	23
3	PIV III	Fever, runny nose, cough, and nasal congestion	23
4	hMPV	Fever, sore throat, and cough	0
5	PIV III	Myalgia, runny nose, sore throat, and cough	0
6	hMPV and FluA	Fever and cough	44
7	PIV III	Myalgia, runny nose, nasal congestion, and cough	21
8	PIV III	Cough and runny nose	0
9	ADV	Fever, myalgia, runny nose, sore throat, and cough	0
10	ADV	Fever, myalgia, and cough	0
11	PIV III	Fever and cough	6
12	RSV and hBOV	Runny nose, nasal congestion, and cough	12
13	PIV III	Runny nose and cough	0
14	PIV III	Fever and cough	0
15	pH1N1, RSV and PIV III	Fever, myalgia, and cough	3
16	FluB	Fever, myalgia, sore throat, and cough	0
17	pH1N1 and hBOV	Fever, myalgia, runny nose, and cough	17
18	hBOV and RSV	Runny nose and cough	0
19	RSV	Coryza, runny nose, sore throat, and cough	0

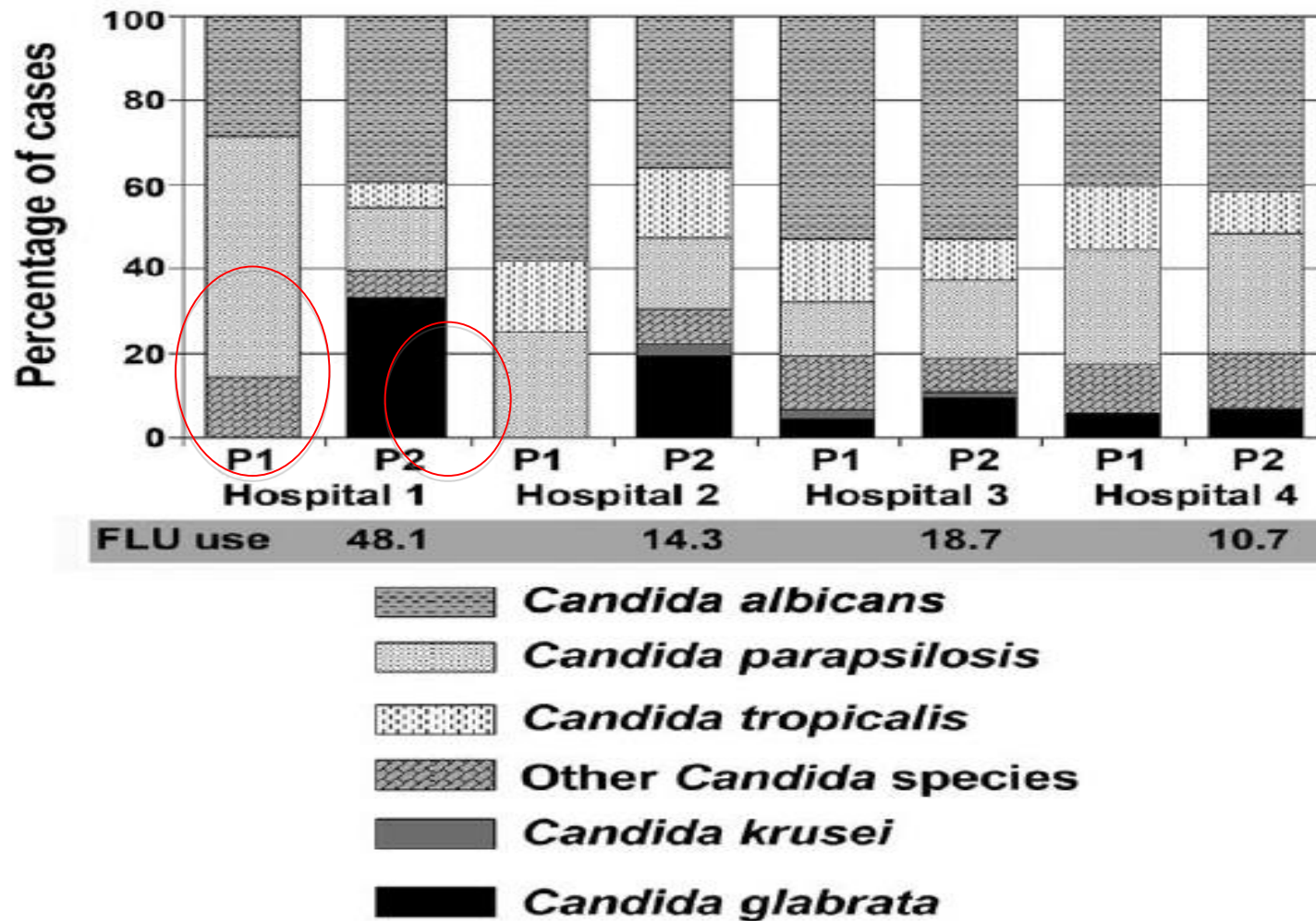
hMPV, human metapneumovirus; RSV, respiratory syncytial virus; PIV III, parainfluenza III virus; FluA, influenza A H3N2; ADV, adenovirus; hBOV, human bocavirus; FluB, influenza B; pH1N1, pandemic influenza A/H1N1.

C.R.A. de Lima, T.B. Mirandoli, L.C. Carneiro, C. Tusset, C.M. Romer, H.F. Andreolla, L.F. Baethgen, A.C. Pasqualotto. Prolonged

Transpl Infect Dis 2014; 16: 165–169

**Prolonged respiratory viral shedding in transplant patients**

## *C. glabrata* no contexto do uso de profilaxia





# Doença de Chagas

**Table 1. Prevalence of *Trypanosoma cruzi* Infection in Organ Transplant Candidates (December 2009)**

Waiting List	Total	Infected	%
Kidney	4949	23	0.46
Liver	563	16	2.84
Lung	95	1	1.05
Heart	94	12	12.77
Kidney-pancreas	89	2	2.25

Source: Instituto Nacional Central Unico Coordinador de Ablación e Implante, 2010.

**Table 2. Prevalence of *Trypanosoma cruzi* Infection in Effective Donors (2005–2009)**

Donors	Total	Infected	%
2005	407	10	2.46
2006	455	17	3.74
2007	486	25	5.14
2008	519	24	4.62
2009	500	23	4.6

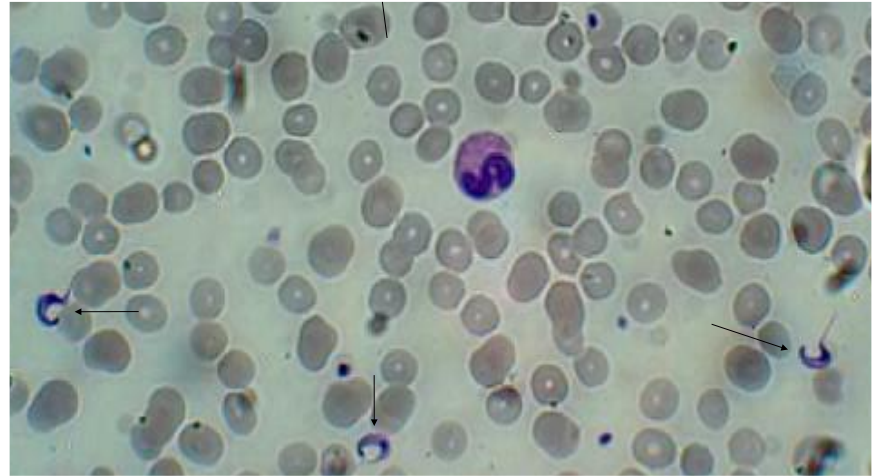
Source: Instituto Nacional Central Unico Coordinador de Ablación e Implante, 2010.

## Chagas' Disease and Solid Organ Transplantation

The Chagas' Disease Argentine Collaborative Transplant Consortium and Domingo Casadei

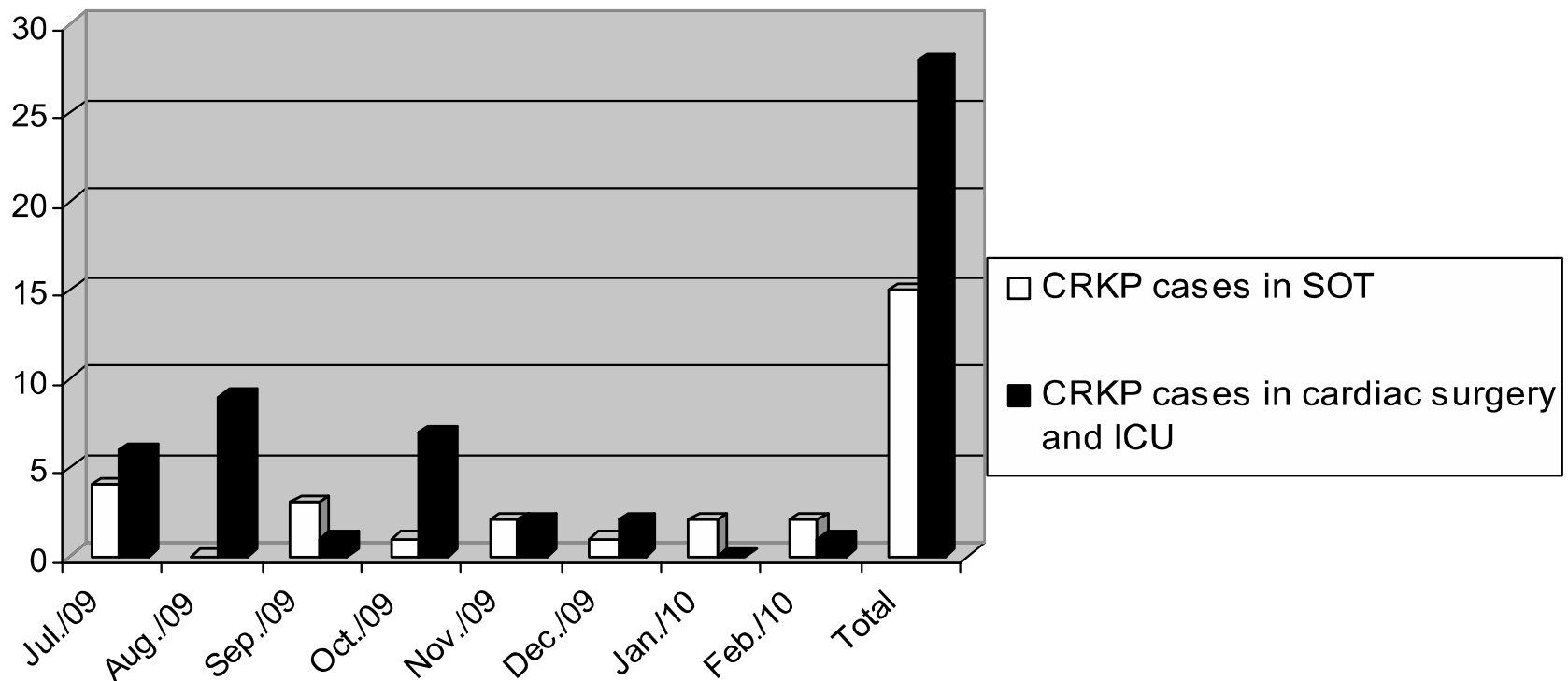
*Transplantation Proceedings*, 42, 3354–3359 (2010)

# Doença de Chagas

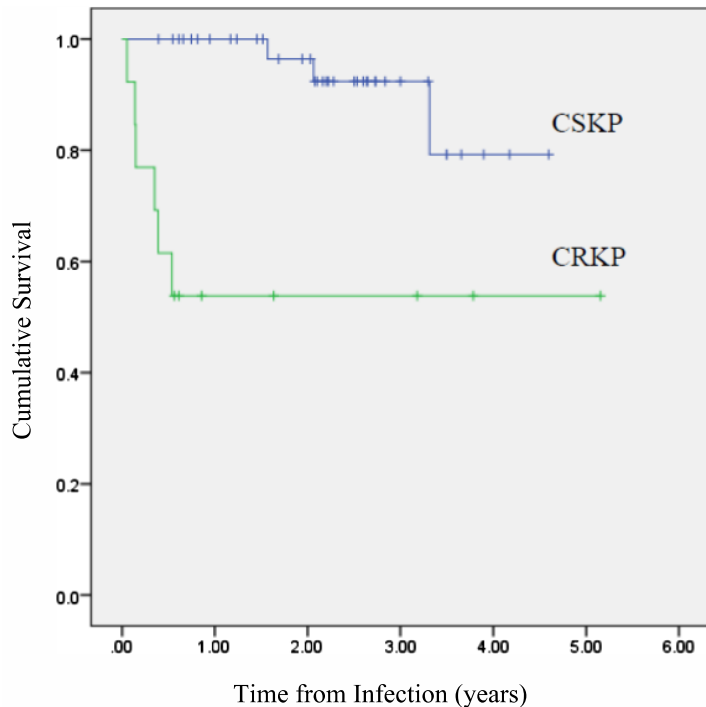


# Enterobactérias Produtoras de Carbapenemases

**Distribution of CRKP Cases of Infection  
Jul/09 - Feb/10**



# Mortalidade



**Fig. 1.** Comparative survival of renal transplant recipients with carbapenem-sensitive *Klebsiella pneumoniae* (CSKP) infection and carbapenem-resistant *K. pneumoniae* (CRKP) infection.

Simkins et al: CRKP in renal transplantation  
*Transplant Infectious Disease* 2014; **16**: 775–782

## Colonization of liver transplant recipients with KPC-producing *Klebsiella pneumoniae* is associated with high infection rates and excess mortality: a case-control analysis

Infection (2014) 42:309–316

Leipzig University Hospital, 04103 Leipzig, Germany

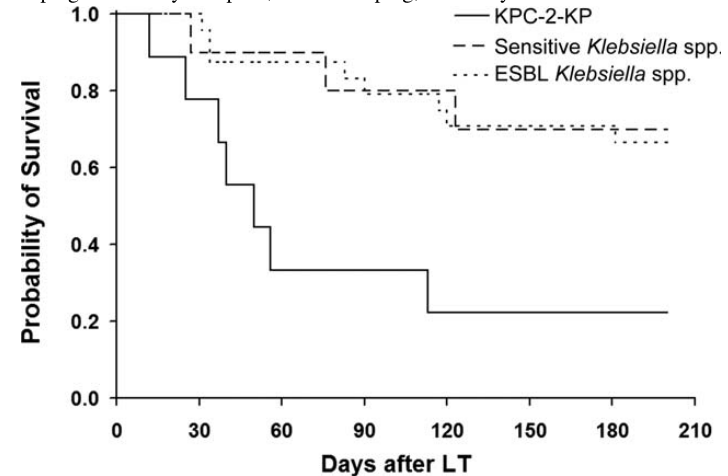
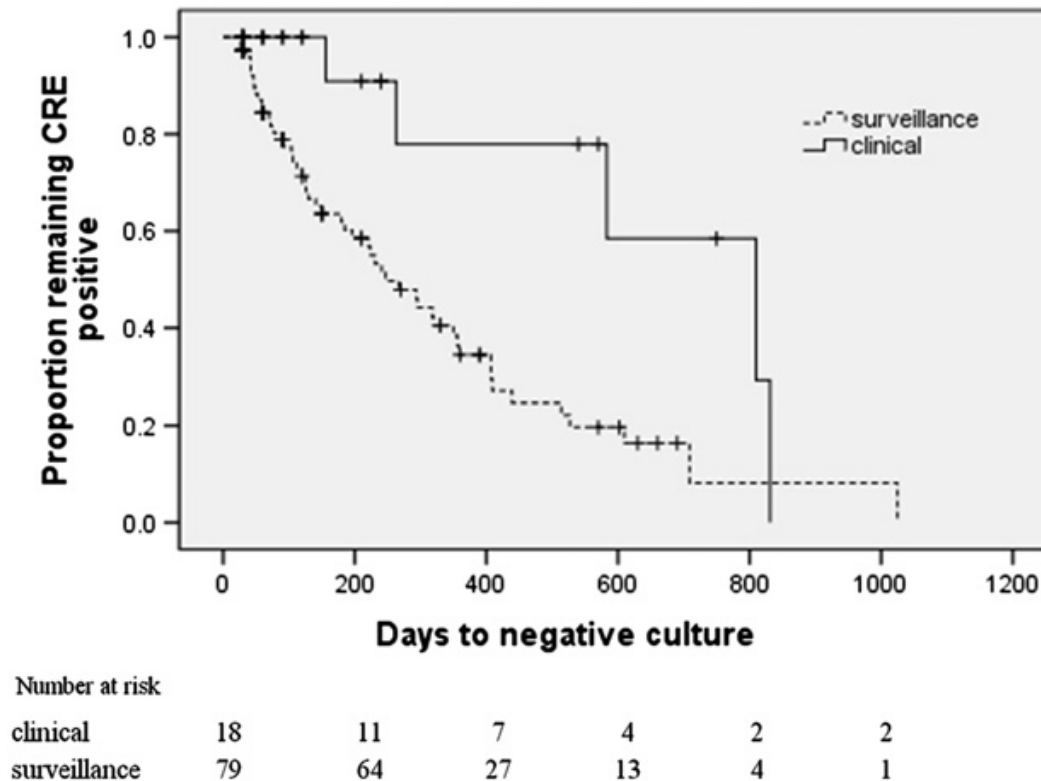


Figure 1. Kaplan-Meier survival curves for LTRs with invasive *Klebsiella* spp. infections. The 6-month survival rate for LTRs with KPC-2-KP was significantly reduced in comparison with the rates for LTRs with sensitive *Klebsiella* strains (sensitive *Klebsiella* spp.,  $P=0.02$ ) and LTRs with ESBL-producing *Klebsiella* strains (ESBL *Klebsiella* spp.,  $P=0.004$ ). Cox-Mantel log-rank statistics, including multiple comparisons with the application of the Holm-Bonferroni method, were used.

- 78% óbitos infectados KPC X 11% controles
- RR: 7,0 (1,8-27,1)

# Tempo de colonização(KPC) (não transplantados)



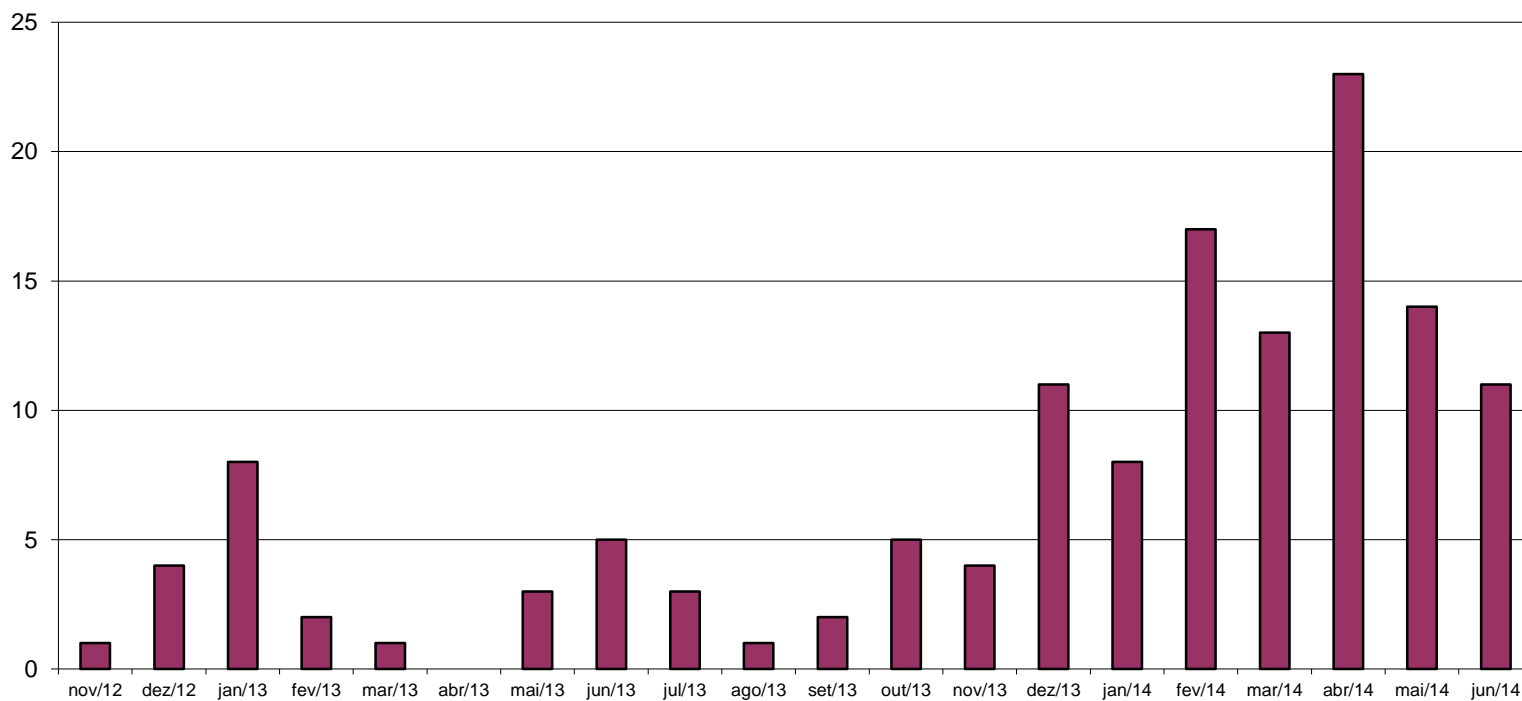
**Fig 2.** Time to negative culture: clinical index culture versus surveillance index culture.



# HDVS

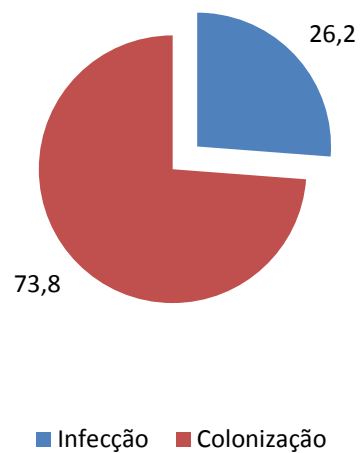


Casos incidentes de EPC  
HDVS (colonização e infecção)

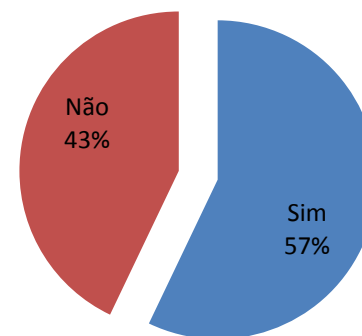




# HDVS



## Mortalidade - Infecção



# Mortalidade por sepse em SOT

- Estudo de caso-controle
- 123 casos- 36% rim 34% fígado
- 246 controles
- SOT com menor risco de morte
- 28 dias- HR 0.22  $p=0,001$
- 90 dias- HR 0,45  $p=0,025$



# Clostridium

- Incidência 0,94%
- Maior em pâncreas
  - Uso de cefalosporina de primeira e segunda geração
  - Uso de corticosteroide até 30 dias antes do Tx
  - Uso de ganciclovir

# Clostridium

Brief report

## *Clostridium difficile* infection in Brazil: A neglected problem?

Renata N. Pires RN<sup>a,b</sup>, Alexandre A. Monteiro BSc<sup>a</sup>, Lilian C. Carneiro PhD<sup>a</sup>,  
Ludmila F. Baethgen PhD<sup>a</sup>, Rejane Tavares PhD<sup>c</sup>, Carla S. Lincho MD<sup>d</sup>,  
Steven Park<sup>e</sup>, David Perlin PhD<sup>e</sup>, Edison M. Rodrigues Filho MD<sup>b,d</sup>,  
Alessandro C. Pasqualotto MD, PhD<sup>a,b,\*</sup>

Multivariate analysis of risk factors for *C difficile* infection

Variables	P value	Odds ratio	95% Confidence interval
Shock septic at presentation	.01	14.6	2.09-102.13
Solid organ transplantation	.04	6.1	1.04-35.63

