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Letter to the Editor

Asymptomatic and symptomatic respiratory virus infection detected in naso-pharyngeal swabs from solid organ transplant recipients early after transplantation

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In transplant recipients, respiratory viral infections (RVI) are associated with high rates of morbidity and mortality.¹ Although recent reports have underlined the increasing importance of RVI in solid organ transplant (SOT) recipients,^{2–6} little is known about its incidence early after transplantation. Immunosuppressive regimens impair SOT recipients' immune system disabling the protection against infections.⁷ In fact, viral pneumonias represent up to 20% of the causes of death among SOT recipients.⁸ We have characterized the incidence of RVI in SOT recipients during the first month post-transplantation using new molecular techniques. Since no virus (es) is associated with one specific syndrome,^{4,9} the identification of RV may be useful for an appropriate infection control and surveillance practices.¹⁰ We performed a prospective study enrolling ninety-eight SOT patients from February 2009 to February 2010. RVI was tested by multiplex-PCR (mPCR; Seeplex-RV12ACE Detection kit, Seegene Inc.) that detects 12 RV (human metapneumovirus, adenovirus, coronavirus 229E/NL63 and parainfluenza 1–3, rhinovirus A/B, coronavirus-OC43/HKU1, respiratory syncytial A–B and influenza A–B). During the first month after SOT the incidence of RVI was relevant at 31.6% (Table 1). Only 5 of these patients (16.1%) were symptomatic, while the rest of patients (26 patients, 83.9%) had an asymptomatic infection with co-infections in 14 of them (53.9%), with influenza A/parainfluenza-2 virus the major cause of co-infection (28.6%). Four of the asymptomatic patients later developed symptoms (5–14 days post testing), thus the overall incidence of symptoms associated with RVI within the first month after transplantation was 9.7% which is higher compared to other studies, probably due to the assay used.^{3,4} We found a high rate of RVI in asymptomatic patients not previously reported probably because most of the studies described RVI during symptomatic episodes.^{3,4,6} The primary overall etiology of RVI was 16.3% influenza A (February–March), 7.1% adenovirus (October), 7.1% coronavirus OC43/HKU1 (March) and 7.1% parainfluenza-2 (March–April). These results are in consonance with other studies showing the highest rate of infection during February and March,⁵ with the majority of the cases associated with influenza A infection, with nearly half of them symptomatic. All patients overcome the infection in the absence of severe symptoms and did not require antiviral administration. The incidence of RVI was not associated with the type of graft (28% in renal transplants, 28.7% in liver recipients, 33.3% in heart recipients). Viral infection was significantly lower in patients receiving triple immunosuppressive

therapy compared to quadruple immunosuppressive therapy (p -value = 0.044, Wilcoxon test, Table 1). In addition, we found higher rates of RVI in patients at high risk for CMV infection (CMV sero-negative recipient that receives a graft from a sero-positive donor; p -value = 0.001, Wilcoxon test).

In addition to mPCR, two additional methods were used for the diagnosis of RVI, viral culture followed by mPCR for the detection of human metapneumovirus, adenovirus, coronavirus 229E/NL63 and parainfluenza 1–3, rhinovirus A/B, coronavirus-OC43/HKU1, respiratory syncytial A–B and influenza A–B and immunofluorescence (IFA, Biotrin-RV Panel, Biotrin-International Ltd.) alone for the detection of adenovirus, influenza A–B, parainfluenza 1–3 and respiratory syncytial virus (Fig. 1). Only 25/98 samples (25.5%) gave identical results using the three assays, demonstrating that mPCR detects more respiratory virus (36.1%) than culture (28.5%) and IFA (3.1%) which is in agreement with previous results.

It is important to consider RVI, especially influenza A virus in immunosuppressed patients since early antiviral therapy in symptomatic cases is associated with improved outcomes. Given the high rate of RVI, measures to avoid nosocomial transmission should be

Table 1
Patient's characteristics.

	No. (%)
Total number of patients	98
Median age [IQR]	52 [57–59.75]
Sex	
Men	59 (60.2)
Women	39 (39.8)
Transplant	
Liver	31 (31.6)
Kidney	61 (62.2)
Heart	6 (6.2)
Main cause of SOT	
Kidney recipients	
Immune disorders	18 (29.5)
Congenital diseases	17 (27.9)
Liver recipients	
Toxic-metabolics disorders	11 (35.5)
Infectious diseases	9 (29.1)
Heart recipients	
Vascular diseases	6 (100.0)
Immunosuppression regimens	
Tacrolimus + MMF + steroids	48 (48.9)
Ciclosporine + MMF + steroids	14 (14.3)
Anti-CD25 + tacrolimus + MMF + steroids	30 (30.6)
Thymoglobulin + tacrolimus + MMF + steroids	6 (6.1)
Patients with symptoms	5 (5.6)
Asymptomatic infections	26 (26.5)
Asymptomatic infections that developed later symptoms	4 (4.1)
Overall incidence of symptomatic RVI within one month after SOT	9 (9.7)
Patients vaccinated against influenza A	61.2%
Vaccinated patients with influenza A symptomatic infection	6.5%

Note: MMF, mycophenolate mophetil; SOT, solid organ transplantation, RVI, respiratory viral infections.

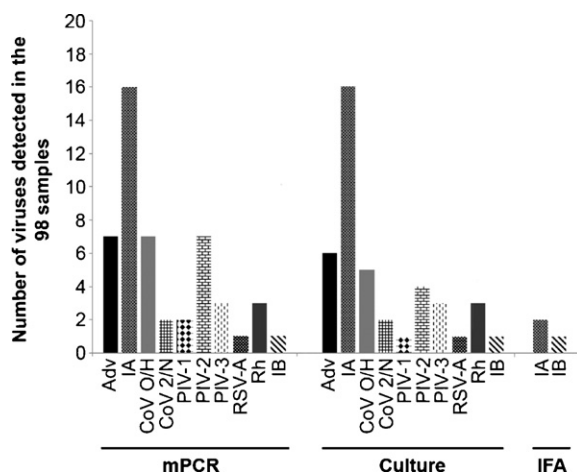


Fig. 1. Incidence of upper-tract respiratory viral infections among SOT patients enrolled in the study obtained by multiplex PCR (mPCR), viral culture (culture) and immunofluorescence (IFA) techniques. The detected viruses were: adenovirus (Adv), influenza A (IA), human coronavirus-OC43/HKU1 (CoV O/H), human coronavirus-229E/NL63 (CoV 2/H), human parainfluenza-1 (PIV-1), human parainfluenza-2 (PIV-2), human parainfluenza-3 (PIV-3), human respiratory syncytial A (RSV-A), human rhinovirus A/B (Rh), influenza B (IB).

rigorous, with infection control measures such as patients isolation and avoidance of contact with symptomatic caregivers. Thus, it may be necessary to increase the vaccination rate among SOT candidates and also close contacts, in order to confer indirect protection for those non-responder to vaccination.

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Conflict of interest

Authors declare no conflict of interest.

Ethical approval

The study was approved by the Virgen del Rocío University Hospital Ethical Committee.

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