27th ECCMID EUROPEAN CONGRESS OF CLINICAL MICROBIOLOGY AND INFECTIOUS DISEASES 22–25 APRIL 2017 VIENNA, AUSTRIA

ESCMID EUROPEAN SOCIETY OF CLINICAL MICROBIOLOGY AND INFECTIOUS DISEASES

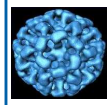
CHU de Liège

Prevalence of norovirus infections and prolonged shedding in symptomatic and asymptomatic kidney transplant patients in a Belgian University Hospital

P.Huynen[1], A.Mauroy[2], L.Weekers[3], L.Magnée[1], L.Bologne[1], C.Bonvoisin[3], R.Boreux[1], F.Toussaint[1], C.Meex[1], MP.Hayette[1], J.Descy[1], E.Thiry[2], P. De Mol[1], P.Melin[1]

[1]Clinical Microbiology, University Hospital of Liège, Belgium, [2]Faculty of Veterinary Medicine, University of Liège, Belgium, [3]Nephrology, University Hospital of Liège, Belgium

BACKGROUND



Noroviruses (NoV) are a leading cause of gastroenteritis worldwide. Moreover, they are recognized as a putative causative agent responsible for prolonged gastrointestinal symptoms in immunosuppressed patients.

OBJECTIVES

We conducted a **prospective study** to determine :

- the prevalence of NoV infection
- the duration of NoV excretion
- the putative impact of a reduction in immunosuppressive therapeutics on gastrointestinal symptoms and on NoV excretion.

STUDY DESIGN

A total of **117 kidney transplant patients** were enrolled in this study from April 2010 to March 2014: 79 and 38 patients with or without gastrointestinal disorders, respectively, at the first visit.

Sampled population: adult kidney transplants patients, presenting or not gastrointestinal troubles, of the University Hospital of Liège, Belgium, a 900-bed clinical hospital.

Clinical and epidemiological data as well as fecal samples were collected. NoV molecular detection and viral load quantification were performed for all samples.

All the patients detected positive for NoV in their first fecal sample were proposed to send back new samples in the following months in the aim to follow the NoV excretion.

Molecular Biology

Viral genomic RNA was automatically extracted with a Maxwell instrument (Promega, Leiden, The Netherlands). Molecular detection of genogroups (G) I, II and IV NoV in stool samples was performed by a home-made real-time RT-PCR[(1)], targeting the ORF1-ORF2 polymerase junction region.

NoV positive samples giving a Ct value below 26 were submitted to molecular characterization.

Financial support: This study was partly financially supported by the Investments Funds for the Scientifically Research provided by the University Hospital of Liège, Liège, Belgium

RESULTS

Clinical & epidemiological data

	Symptomatic patients (n=79)		Asymptomatic patients (n=38)		
	N	Number (%)	N	Number (%)	p value
Age (years)					
Mean ±SD	79	52.1 ± 14.2	38	52.8 ± 10.4	0.78
<30		6 (7.6)		1 (2.6)	
30-39		11 (13.9)		4 (10.5)	
40-49		20 (25.3)		10 (26.3)	
50-59		15 (19)		13 (34.2)	
60-69		21 (26.6)		8 (21.1)	
70-79		6 (7.6)		2 (5.3)	
Sex					
	79		38		0.41
Male		50 (63.3)		21 (55.3)	
Female		29 (36.7)		17 (44.7)	
Delay from transplant					
Median (Q1-Q3)	79	19.5 (5.4-60.9)	38	38.2 (24.2-71)	0.083
< 6 m.		24 (30.4)		5 (13.2)	
6 m. – 1 year		7 (8.9)		1 (2.8)	
1 – 5 years		27 (34.2)		19 (50)	
> 5 years		21 (26.6)		13 (34.2)	
Symptoms					
	79		NA		
Diarrhoea		73 (92.4)			
Vomits		11 (13.9)			
Abdominal pain		33 (41.8)			
Fever		7 (8.9)			

(NA : not applicable, m: months)
Table I. Epidemiological and clinical data of symptomatic and asymptomatic kidney transplant patients.

Molecular diagnosis of norovirus and genogrouping

		NoV detection			Genogrouping		
	Total	Negative	Positive		GI/IV	GII	
Patients	N	Number (%)	Number (%)	p value	Number (%)	Number (%)	p value
Symptomatic	79	34 (81.0)	15 (19.0)	0.25	1 (6.7)	14 (93.3)	0.39
Asymptomatic	38	34 (89.5)	4 (10.5)		1 (25.0)	3 (75.0)	
Total	117	98 (83.8)	19 (16.2)		2 (10.5)	17 (89.5)	

Table II. Results of NoV detection and genogrouping by real time RT-PCR in kidney transplant patients.

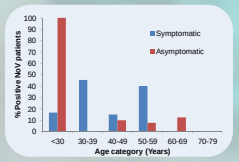


Figure 1. Proportion of detected NoV by real time RT-PCR by age category in kidney transplant patients

NoV GII was the most prevalent genotype in both groups.
In both symptomatic (SP) et asymptomatic (AP) patients, the presence of NoV was lower in older patients (OR=0.95, p=0.013) (Fig.1).

The mean log of viral loads for NoV GII did not differ between the groups SP and AP (p=0.67) (Table III).

		NoV detection		
	Total	GI/IV	GII	
Patients	N	Mean viral load (copies/ml)	Mean viral load (copies/ml)	p value GII
Symptomatic	79	2074 ± 0	6507 ± 5710	0.67
Asymptomatic	38	439 ± 0	77252 ± 194530	

Table III. NoV mean viral loads in kidney transplant patients

Duration of NoV excretion

Ref. patient	Date 1st NoV PCR positive sample	Date late NoV PCR positive sample	NoV excretion duration (days)	Date late NoV PCR negative sample	Maximal NoV excretion duration (days)
Symptomatic patients					
3	11/05/2010	191/2011	253	NA	≥253
9	10/03/2011	2/8/2011	146	NA	≥145
12	8/06/2011	NA	NA	NA	NA
19	8/04/2011	NA	NA	NA	NA
20	5/10/2012	NA	NA	8/10/2012	3
26	28/1/2011	NA	NA	27/06/2012	516
34	29/12/2012	NA	NA	NA	NA
36	6/02/2013	9/7/2013	156	NA	≥153
46	30/05/2013	NA	NA	NA	NA
51	2/06/2010	NA	NA	17/11/2010	168
54	4/05/2010	11/8/2010	97	16/8/2011	469
60	17/04/2012	NA	NA	8/5/2013	386
63	28/07/2010	12/8/2010	15	NA	≥15
68	7/02/2012	NA	NA	14/2/2012	7
70	22/12/2010	NA	NA	8/7/2013	929
Asymptomatic patients					
88	11/12/2012	9/7/2013	211	NA	≥210
93	8/03/2013	NA	NA	29/8/2013	174
96	4/04/2013	NA	NA	27/5/2013	174
97	25/04/2013	NA	NA	NA	≥50

(NA : not applicable)
Table IV. NoV follow-up in kidney transplant patients

Patient	Duration NoV shedding (days)	Stool collection date	Ct	Viral load (copie/ml)	Log copie	Genotype
36/ symptomatic	153	6/2/13	24	229 469	5.36	GII.4
		5/3/13	25	92 136	4.96	
		29/4/13	22	849 979	5.93	
		9/7/13	39	7.2	0.85	
88/ asymptomatic	211	11/12/12	28	11 112	4.05	GII.12
		4/4/13	23	483 739	5.68	
		9/7/13	29	7402	3.87	

(Ref: reference number of the patient, Ct: cycle threshold)
Table V. NoV genotyping

Prolonged NoV excretion was documented in both SP and AP who received a NoV follow-up (Table IV).

Phylogenetic analysis in follow-up samples from 1 SP and 1 AP presented prolonged NoV excretion identified a GII.4 and a GII.12 strain respectively. Molecular NoV characterization confirmed the presence of a single genotype within each patient (Table V).

Immunosuppressive treatment (IT)

Symptomatic patients

↓ IT doses: 9/15 patients
- Improvement of the symptoms in all
- ↓ NoV viral loads in the 6 patients who gave a follow-up sample

No ↓ IT doses: 6/15 patients
- Improvement of the symptoms in 4/6 patients
- ↓ NoV viral loads in the 2 patients who gave a follow-up sample

Asymptomatic patients

↓ IT doses: 0/4 patients

No ↓ IT doses: 4/4 patients
↓ NoV viral loads in the patient who gave a follow-up sample

CONCLUSION

NoV is a major viral enteric pathogen identified in transplant patients.

In our prospective study, we described the clinical presentation and the prevalence of NoV among 117 adult kidney transplant patients presenting or not gastrointestinal disorders, with prevalence rate of 19% and 11% in each patients group respectively.

We highlighted a prolonged NoV excretion in both symptomatic and asymptomatic kidney transplant patients.

When reduction of immunosuppressive treatment was applied, a decrease in NoV viral loads as well as improvement of the symptoms were observed in thesymptomatic patients group.

Continued investigation will allow the understanding of the NoV impact in immunosuppressed patients.

Bibliography

(1) Stals A. et al, Journal of Virological Methods. 2009;161:247–253

P1918

P.Huynen@chu.ulg.ac.be