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Impact and Performance of RT-PCR for Norovirus Detection and Outbreak Management

Literature Review


Epidemiology


Economic Impact of Norovirus Outbreaks


Guidelines


Performance of RT-PCR


Performance of ELISA vs. RT-PCR


Impact

PUBLICATIONS

1

Ennuschat N, Härtel S, Pietsch C, Liebert UG. **Norovirus Epidemiology and Genetic Diversity in Leipzig, Germany during 2013-2017.** Viruses. 2021 Sep 29;13(10):1961. doi: 10.3390/v13101961. PMID: 34696390; PMCID: PMC8541062. (2021)

- Genogroup I norovirus infections being more frequently community-acquired than nosocomial is consistent with the fact that GGI noroviruses are more likely to be foodborne than person-borne.
- The distribution of community-acquired (51.7%) and nosocomial (48.3%) infections in the study was similar to results obtained in a study covering all of Germany.
- Norovirus RNA was detected in 611 out of 7509 (8.1%) samples. GII.4 as the overall most present genotype, but also showing differences in occurring genotypes regarding age and the setting of the infection. Generally, children under five years of age are less prone to nosocomial infection, and GII.3 as well as GII.6 were especially frequent in this cohort. Rise in norovirus infections with GII.2 [P16] during the season 2016/2017 in Germany.

2

Hofmann FM, Olawumi E, Michaelis M, Stößel U, Hofmann F. **Significance of norovirus in occupational health: a review of published norovirus outbreaks in Central and Northern Europe. Int Arch Occup Environ Health.** 2020 Nov;93(8):911-923. doi: 10.1007/s00420-020-01543-4. Epub 2020 May 1. PMID: 32358716; PMCID: PMC7222890. (2020)

- More than 50% of the Norovirus (NoV) cases during 13 out of 43 outbreaks in health care facilities were employees and those staff members accounted for 34.9% of the NoV cases during community facility outbreaks.
- NoV should thus be regarded as important occupational disease for staff in the former group of settings. Regarding the prevention of NoV outbreaks, the study strongly advocates the implementation of additional precautions, such as dedicated personnel concepts for NoV outbreaks, to increase the compliance with existing prevention strategies as exclusion policies. The resulting costs should always be viewed relative to significantly higher expenses associated with uncontrolled NoV outbreaks.
- Norovirus outbreaks lead to significant economic losses due to revenue losses and microbiological testing. Employees in hospitals and community facilities seem quantitatively to be most vulnerable towards norovirus epidemics. Therefore, high quality of prevention measures in these settings and respective compliance with prevention strategies should have the highest priority.

3

Sandmann FG, Shallcross L, Adams N, Allen DJ, Coen PG, Jeanes A, Kozlakidis Z, Larkin L, Wurie F, Robotham JV, Jit M, Deeny SR. **Estimating the Hospital Burden of Norovirus-Associated Gastroenteritis in England and Its Opportunity Costs for Nonadmitted Patients.** Clin Infect Dis. 2018 Aug 16;67(5):693-700. doi: 10.1093/cid/ciy167. PMID: 29529135; PMCID: PMC6094002. (2018)

- Between July 2013 and June 2016, 17.7% of primary and 23.8% of secondary gastrointestinal diagnoses were norovirus attributable. Annually, the estimated median 290,000 occupied and unoccupied bed-days used for norovirus displaced 57,800 patients. Conventional costs for the National Health Service reached £107.6 million; the economic burden approximated to £297.7 million and a loss of 6,300 quality-adjusted life-years annually.
- Norovirus-associated gastroenteritis ties up the equivalent of more than twice the daily hospital bed stock in England, with a substantial economic and health impact for the NHS and patients.
- In England, norovirus has become the second-largest contributor of inpatient gastrointestinal illnesses in England since mid-2013. With the projected impact being greater than previously estimated, improved capture of relevant opportunity costs seems imperative for diseases such as norovirus.

PUBLICATIONS

4

Navas E, Torner N, Broner S, Godoy P, Martínez A, Bartolomé R, Domínguez A; Working Group for the Study of Outbreaks of Acute Gastroenteritis in Catalonia. **Economic costs of outbreaks of acute viral gastroenteritis due to norovirus in Catalonia (Spain), 2010-2011.** BMC Public Health. 2015 Oct 1;15:999. doi: 10.1186/s12889-015-2289-x. PMID: 26424707; PMCID: PMC4589948. (2015)

- Twenty-seven outbreaks affecting 816 people in closed institutions and 74 outbreaks affecting 1,940 people in the community were detected. The direct and indirect costs of outbreaks were € 131,997.36 (€ 4,888.79 per outbreak) in closed institutions and € 260,557.16 (€ 3,521.04 per outbreak) in community outbreaks. The cost per case was € 161.76 in outbreaks in closed institutions and € 134.31 in community outbreaks. The main costs were surveillance unit monitoring (€ 116,652.93), laboratory diagnoses (€ 119,950.95), transport of samples (€ 69,970.90), medical visits (€ 25,250.50), and hospitalization (€ 13,400.00).
- The lack of widespread availability of laboratory confirmation RT-PCR technique makes it necessary to transport case samples from place of outbreak occurrence to the public health laboratory. This fact increases outbreak investigation expense.
- Urgent reporting of outbreaks would allow the implementation of control measures that could reduce the numbers affected and the duration of the illness and thus the costs derived from them. Norovirus testing by RT-PCR and confirmation should be more readily available to microbiology laboratories enhancing detection of sporadic cases that are now underdetected.

5

Chadwick PR, Trainor E, Marsden GL, Mills S, Chadwick C, O'Brien SJ, Evans CM, Mullender C, Strazds P, Turner S, Weston V, Toleman MS, de Barros C, Kontkowski G, Bak A. **Guidelines for the management of norovirus outbreaks in acute and community health and social care settings.** J Hosp Infect. 2023 Jun;136:127-191. doi: 10.1016/j.jhin.2023.01.017. Epub 2023 Feb 15. PMID: 36796728. (2023)

- It is good practice, where resources allow to test all symptomatic patients for norovirus infection. Testing may have benefits in both outbreak and non-outbreak situations. Testing all symptomatic individuals may help to define an outbreak or even prevent an outbreak from occurring if the initial cases are promptly identified and managed. During outbreaks, testing can help to identify positive cases so that the control measures (i.e., isolation or cohorting) can be applied. This may be particularly important in acute settings where some patient populations (i.e., patients cared for on gastrointestinal wards) may demonstrate symptoms compatible with norovirus infection.
- Moderate evidence that PCR (single or multiplex) testing is more sensitive compared with other tests for detecting norovirus. Due to low sensitivity of non PCR-tests, the Working Party stressed that, where negative results are obtained, there is still a need to confirm the absence of norovirus by PCR testing.
- Wherever possible, test all symptomatic patients to establish whether their symptoms are due to norovirus infection. Wherever possible, use PCR (single or multiplex) for confirmation of presence or absence of norovirus infection. Do not use enzyme or immunochromatography tests as a sole negative test to exclude cases of norovirus.

PUBLICATIONS

6

Gonzalez MD, Langley LC, Buchan BW, Faron ML, Maier M, Templeton K, Walker K, Popowitch EB, Miller MB, Rao A, Liebert UG, Ledeboer NA, Vinjé J, Burnham CA. **Multicenter Evaluation of the Xpert Norovirus Assay for Detection of Norovirus Genogroups I and II in Fecal Specimens.** J Clin Microbiol. 2016 Jan;54(1):142-7. doi: 10.1128/JCM.02361-15. Epub 2015 Nov 11. PMID: 26560532; PMCID: PMC4702714. (2016)

- For both prospective and frozen specimens, the Xpert® Norovirus test showed positive percent agreement (PPA) and negative percent agreement (NPA) values of 98.3% and 98.1% for GI and of 99.4% and 98.2% for GII, respectively. Norovirus prevalence in the prospective specimens was 9.9% (n90), with the majority of positives caused by genogroup II (82%, n74). The positive predictive value (PPV) of the Xpert Norovirus test was 75% for GI-positive specimens, whereas it was 86.5% for GII-positive specimens. The negative predictive values (NPV) for GI and GII were 100% and 99.9%, respectively.
- Efficient and accurate testing has the potential to rapidly identify infected individuals, minimizing the need for additional diagnostic testing and prompting infection prevention measures.
- Xpert Norovirus test is a rapid and accurate method to detect and differentiate the prominent norovirus genogroups.

7

Sato Y, Nirasawa S, Saeki M, Yakuwa Y, Ono M, Yanagihara N, Fujiya Y, Takahashi S. **Evaluation of two commercial molecular diagnostic assays: The Xpert Norovirus and the TRCReady NV.** J Infect Chemother. 2021 Jul;27(7):1115-1118. doi: 10.1016/j.jiac.2021.02.004. Epub 2021 Apr 1. PMID: 33814351. (2021)

- Total concordance rate were all 100.0% for Xpert Norovirus, and 96.0%, 100.0%, and 98.3%, respectively, for TRCReady NV. Xpert Norovirus results were completely consistent with the real-time RT-PCR results, whereas only one result of TRCReady NV was false-negative. With the implementation of Xpert Norovirus in February 2016, the turn-around time (TAT) dramatically decreased and the period to comply specimens was extended from 9 a.m. to 4 p.m.
- With the implementation of Xpert Norovirus in February 2016, the turnaround time (TAT) dramatically decreased.
- In conclusion, norovirus detection by Xpert Norovirus and TRCReady NV is highly useful for diagnosis and infection control because these tests are easy to operate, quick, and exhibit almost the same performance as that of real-time RT-PCR.

8

de Bruin E, Duizer E, Vennema H, Koopmans MP. **Diagnosis of Norovirus outbreaks by commercial ELISA or RT-PCR.** J Virol Methods. 2006 Nov;137(2):259-64. doi: 10.1016/j.jviromet.2006.06.024. Epub 2006 Aug 9. PMID: 16901556. (2006)

- A sensitivity of 38% was found for the Dako kit, similar to a previous observation. A sensitivity and specificity of 36% and 88% were found for the RIDASCREEN kit, which is comparable to the Dako kit.
- At least 40% of the NoV outbreaks would not be diagnosed as NoV outbreaks using any of the two commercial ELISAs evaluated.
- EIA tests are not suitable for diagnosis of infection in individual patients, or for genotype assignment. Because of the low sensitivity, RT-PCR remains the “gold standard” for routine diagnosis of NoV in samples from patients with gastroenteritis.

PUBLICATIONS

9

Dewar S, Vass D, MacKenzie FM, Parcell BJ. **Point-of-care testing by healthcare workers for detection of meticillin-resistant Staphylococcus aureus, Clostridioides difficile, and norovirus.** J Hosp Infect. 2019 Dec;103(4):447-453. doi: 10.1016/j.jhin.2019.08.002. Epub 2019 Aug 9. PMID: 31404566. (2019)

- Xpert Norovirus sensitivity was 83.33%, specificity 98.66%, PPV 71.43% and NPV 99.32% compared to reference-standard detection by laboratory PCR method.
- The test significantly reduced hands-on time, process steps, and time to result for identification of norovirus. Overall agreement with central laboratory testing was >98%. Staff members fed back that POCT had a positive impact in terms of clinical utility.
- Xpert Norovirus can be used as POCT solely by HCWs in a ward setting. Each test was used throughout a 7 day/24 h period with potential positive impact on bed management and patient care.

10

Salmona M, Jolivet S, Duprilot M, Akpabie AC, Fourati S, Decousser JW. **Laboratory-based strategy using a new marketed polymerase chain reaction assay to manage diarrheic episodes among patients from rehabilitation and long-term care facilities.** Am J Infect Control. 2016 Jun 1;44(6):716-8. doi: 10.1016/j.ajic.2015.12.027. Epub 2016 Feb 24. PMID: 26921013. (2016)

- Positive Cd PCR was obtained for 9 of the 52 patients (17%). The Nv PCR performed for all of the Cd-negative specimens was positive in 10 of 43 (23%) patients (all GII). This 2-step laboratory based strategy seems to be economical and efficient: the 37% positive rate was similar to the 37.8% of tests identifying a single infectious agent in a recent large European study.
- Early detection of sporadic NV cases during the seasonal period cost-effectively prevents outbreaks. Within a maximum TAT of 3 hours, this approach could accurately identify the 2 main infectious agents responsible for gastroenteritis outbreaks.
- This study underlines the significant contribution of a laboratory-based strategy, including Xpert Norovirus, to adequately implement isolation precautions for diarrheic patients from RCFs and LTCFs.

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