SIGNIFICANCE OF RECENT UNPREDICTED RISE OF COINCIDENTAL FINDING OF BOCAVIRUS DURING RAPID COVID-19 SCREENING

MAIN AUTHOR: JAMES BURTON CO-AUTHOR: DR JAMES HATCHER

GREAT ORMOND STREET HOSPITAL CHARITY

Abstract

Great Ormond Street Hospital (GOSH), a tertiary paediatric centre serves a wide range of patients with specific and complex medical conditions from a wide and vast global demographic. Routine screening for respiratory viruses in this patient population even prior to the COVID-19 pandemic is nothing new. The department has three QIAstat Diagcore instruments used for rapid respiratory testing, which include a combination of viral and bacterial targets associated with respiratory infection. Originally introduced for full, rapid and out of hours respiratory viral screening for PICU patients, during the pandemic has regularly been used for the rapid screening for SARS-CoV-2. This has led to several coincidental positive results for other respiratory targets including Human Bocavirus.

Introduction

Human Bocavirus (HBoV) was first identified in 2005 and belongs to the Paroviridae family. HBoV are non-enveloped, single stranded DNA viruses and there are four identified Bocaviruses (HBoV1-4). It is the HBoV-1 virus which is associated with a wide range of respiratory clinical syndromes in young children especially (6-24 months of age) such as common cold, pneumonia, bronchiolitis and asthma exacerbations. Despite evidence strongly suggesting the pathogenicity of HBoV in causing mild to severe respiratory tract infections in children, its clinical significance and therefore effect of infection control processes and management in the hospital setting remains a subject for discussion. This is in part due to a lack of study into the pathogeneses of the virus due to a lack of specific cell lines for virus culture or experimental animal models.

The discussion around the clinical significance of a HBoV positive result in a respiratory tract sample (e.g., Nasopharyngeal aspirate) focuses around two key areas;

1. HBoV DNA can remain detectable in samples from the respiratory tract for up to 12 months after primary infection
2. HBoV DNA has been detected in many asymptomatic children also.

Due to the nature of the patients treated GOSH, who often have highly complex and specific clinical conditions including substantial immunosuppression, leaves them susceptible to a range of respiratory viral infections. Routine respiratory virus screening of nasopharyngeal aspirates is imperative for early detection of respiratory viruses to ensure health of individual patients but also to avoid outbreaks amongst shared wards/ clinical areas.

HBoV in focus at GOSH

Positive results for respiratory viruses for inpatients at GOSH (symptomatic or not) has multiple effects infection control and patient management within the hospital; these patients may have surgical/ treatment procedures postponed as a result or/ and may need to be isolated from other patients (side rooms).

After a rise in recent cases of positive HBoV result in inpatients Microbiology Consultants requested a review of the results. This included:

- Review of symptomatic/ asymptomatic (co-incidental finding)
- Identify patients with co-infection with other respiratory viruses (RSV, Rhinovirus/Enterovirus etc)
- Retesting HBoV positive samples on a different platform
- Reason for screening (i.e., respiratory viral screen or COVID-19 screen)

Methods

1. Samples from patients with a QIAstat Diagcore positive result for HBoV DNA (inpatients only) tested for HBoV DNA via separate method (Luminex NxTag assay) at external laboratory.
2. Clinical information collected regarding presence or absence of respiratory illness, reason for use of the test rather than dedicated asymptomatic COVID-19 screening test method available.
3. Comparability of results from both platforms analysed and decision regarding current significance of positive result in asymptomatic patients analysed.

Results

As shown in table 1, greater than 75% of patients with HBoV positive using QIAstat Diagcore had no respiratory symptoms related to suspicion of respiratory viral infection. The majority of these HBoV positive results were coincidental findings when the QIAstat Diagcore instrument was used for an urgent COVID-19 screen. Less than half of these positive results (37%) were confirmed by second testing platform (Luminex NxTag assay).

Table 1: QIAstat vs NxTag assay vs symptomatic status

QIAstat Diagcore		Luminex NxTag assay	Symptom Status
Bocavirus DNA result	Other respiratory virus detected?		
Detected	No	Not Detected	**Asymptomatic**
Detected	No	Not Detected	**Asymptomatic**
Detected	No	Not Detected	**Asymptomatic**
Detected	No	Not Detected	**Asymptomatic**
Detected	No	Not Detected	**Asymptomatic**
Detected	No	Not Detected	**Asymptomatic**
Detected	**No**	**Not Detected**	**Symptomatic**
Detected	No	Detected	**Asymptomatic**
Detected	No	Not Detected	**Asymptomatic**
Detected	Rhino/Entero	Detected	**Asymptomatic**
Detected	Parainfluenza 3	Not Detected	**Asymptomatic**
Detected	No	Not Detected	**Asymptomatic**
Detected	**No**	**Detected**	**Symptomatic**
Detected	Rhino/Entero	Detected	**Asymptomatic**
Detected	**RSV AB**	**Detected**	**Symptomatic (RSV +)**
Detected	No	Detected	**Asymptomatic**

Table 2: Concordance between methods by Ct value on QIAstat Diagcore

HBoV Ct on QIAstat	HBoV NxTag assay result	Concordance between methods
Ct < 26	3/3	100%
Ct 26-33.9	2/7	28%
Ct >/= 34	1/6	14.29%

Table 3: Concordance between methods by End Point Fluorescence value on QIAstat Diagcore

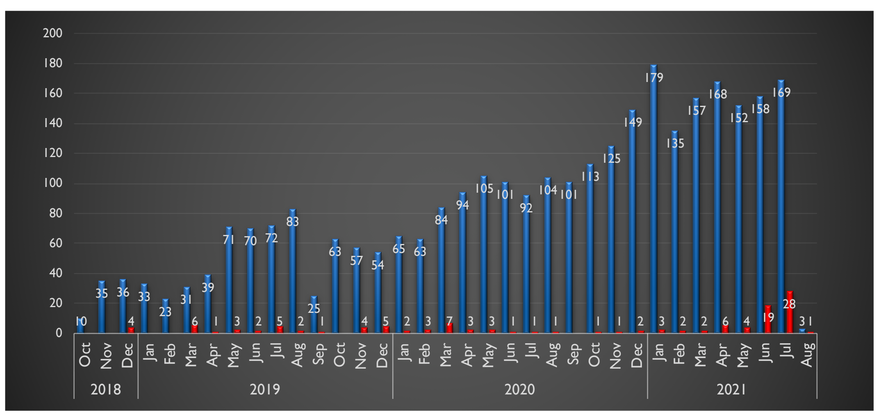
HBoV EPF on QIAstat	HBoV NxTag assay result	Concordance between methods
EPF <50,000	3/4	75%
EPF 50,000-100,000	2/8	25%
EPF >100,000	1/4	25%

Overall Concordance between methods

37.5%

Table two shows comparability of results between two methods when results were further broken down and grouped by cycle threshold (Ct) on QIAstat. A QIAstat HBoV Ct result of less 26 had 100% concordance with result the NxTag assay. The comparability between the two methods was also compared using the end point fluorescence (EPF) value from the QIAstat instrument as this seemed to vary regardless of Ct value. The comparability was 75% for results with an EPF of <50,000, but dramatically decreased for those results with an EPF of >50,000.

HBoV positives vs number of tests at GOSH by month/year



Graph 1: Number of QIAstat requests vs number of HBoV positives at GOSH between 2018-2021

The graph above shows the number of QIAstat requests (**blue**) vs the number of HBoV positive results (**red**) by month between 2018 (QIAstat instrument introduced into the department) and August 2021. It is clear to see the number of requests for QIAstat respiratory virus testing have gone up year on year with an increase in HBoV positive results peaking especially in 2021. However, this data does not consider the QIAstat being used for rapid COVID-19 screening and the HBoV positive results being a coincidental finding and in addition does not differentiate symptomatic from asymptomatic cases.

Conclusions

Clinical significance of HBoV positive results in asymptomatic patients doubtful but has an important impact with regards to infection control and patient management/ movement Pending full and decisive evidence of the significance positive Bocavirus results to be supressed in asymptomatic patients. At this current time this is also supported due to the substantial difference in the concordance of results between the two different testing platforms/ assays. The introduction of a separate rapid assay/ platform for urgent COVID-19 screen is also expected to lower the number of coincidental respiratory viruses such as HBoV. There is no doubt further work regarding the significance of HBoV as a pathogen in human health and its implications on infection control needs further work.

References

Christensen, A., Kesti, O., Elenius, V., Eskola, A., Døllner, H., C, A., . . . Jartti, T. (2019). Human bocaviruses and paediatric infections. Lancet Child Adolescent Health, 418-426.

Guido, M., Tumolo, M., Verri, T., Romano, A., Serio, F., De Giorgi, M., . . . Zizza, A. (2016). Human bocavirus: Current knowledge and future challenges. World J Gastroenterol, 8684-8697.

Jiang, W., Yin, F., Zhou, W., Yongdong, Y., & Ji, W. (2016). Clinical significance of different virus load of human bocavirus in patients with lower respiratory tract infection. Scientific Reports.

Longtin, J., Bastien, M., Gilca, R., Leblanc, E., De Serres, G., Bergeron, M. G., & Boivin, G. (2008). Human bocavirus infections in hospitalized children and adults. Emerging infectious diseases, 217-221.

Lüsebrink, J., Wittleben, F., Schildgen, V., & Schildgen, O. (2009). Human bocavirus - insights into a newly identified respiratory virus. Viruses, 3-12.

Acknowledgements

Dr John Hartley MRCP FRCPath

Francis Yongblah BSc MSc FIBMS