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Genomic subtyping advances our understanding of the epidemiology of campylobacteriosis: a study from Nova Scotia, Canada

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Introduction

- Campylobacter is a common community cause of diarrhea and enteric infection can have serious sequelae.
- Detection of outbreaks is suboptimal because of a lack of standardized typing
- Comparative Genomic Fingerprinting (CGF40) is a recently described typing method which has been shown to be discriminatory for Campylobacter spp.
- We compared public health data with CGF40 typing results to determine the role of CGF40 in detection of outbreaks, and possible sources of infection with Campylobacter in NS

Methods

At our request, between Jan 1 2012 and Mar 31 2015, Campylobacter isolates isolated at or sent to the Central Zone laboratory from laboratories around the province were stored at the central laboratory at -70C. Isolates were shipped periodically to NML Lethbridge for CGF40 typing. For CGF40 typing, 8 multiplex PCR reactions were performed on each isolate as previously described (Taboada et al 2012). The presence or absence of amplicons for 40 genes were converted to binary results and analysed using Bionumerics software.

Cases of Campylobacter infection are investigated by NS Public Health services and a standard questionnaire is completed routinely. For the study, the questionnaires were reviewed retrospectively and clusters identified by temporal, social and spatial associations. A case-case analysis was done to compare particular types with sporadic isolates to compare exposures. CGF40 clusters with 5 or more cases were tested for associations with the following risk factors: urban residence, acquisition of illness in NS, age, sex, work in chicken or mink farming/processing, contact with chickens, unpasteurized milk, pet dog and/or cat, recreational water, farm/zoo/wildlife animals.

Selected References:

Taboada E et al 2012. Journal of Clinical Microbiology 50(3) 788-797.
Clark C et al 2012. Journal of Clinical Microbiology 50(3) 798-809.
Taboada et al 2013. J. Microbiological Methods. 95 24-31.

Results

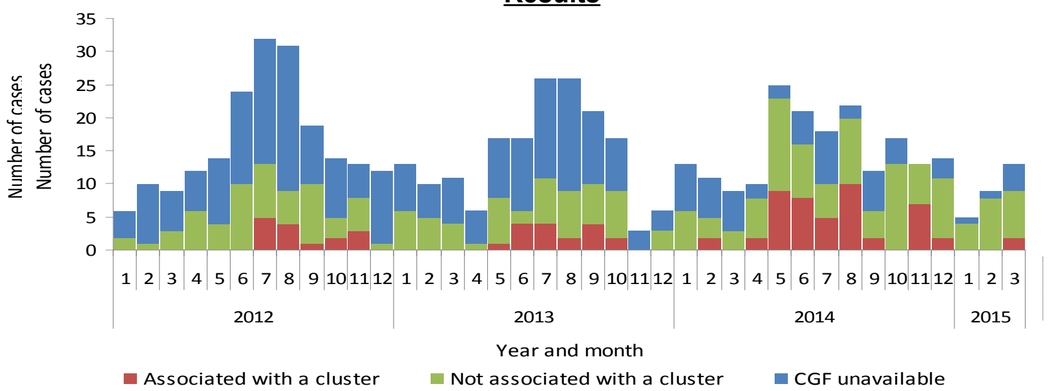

Fig 1. Reported Cases of Campylobacteriosis and association with temporal CGF40 Clusters 1/12-3/15 (n=581)

CGF40 Type	Number Of Isolates	Species	Years isolated*	No. Clusters (Pts within 30 days)	Recent Travel History
0083.001.002	17	jejuni	2012-2015	1 (9)	within Canada
0018.001.002	14	jejuni	2012-2015	3 (3,2,2)	multiple countries/continents
0253.004.001	12	jejuni	2012, 2014, 2015	3 (3,2,2)	within Canada
0044.003.001	8	jejuni	2012-2014	2 (2,2)	none
0082.001.001	7	jejuni	2012-2015	1 (2)	within Canada
0633.004.002	7	coli	2013, 2014	1 (3)	multiple countries/continents
0169.001.002	7	jejuni	2012-2014	1 (2)	within Canada
0173.002.004	6	jejuni	2012, 2014	1 (2)	none
0882.005.001	6	jejuni	2012-2014	1 (2)	within Canada
0960.007.001	6	jejuni	2014	1 (2)	none
0926.002.001	6	jejuni	2012, 2014	1 (3)	within Canada
0922.001.002	6	jejuni	2012	1 (3)	within Canada
0129.001.002	6	jejuni	2014	2 (2,2)	Cuba
0117.001.001	6	jejuni	2012-2014	1 (2)	Dominican Republic
0083.007.001	5	jejuni	2013, 2014	1 (2)	multiple countries/continents

Table 1. Frequency of common CGF40 subtypes and associated clusters.

- Blinded CGF40 typing was able to discern known epidemiologically-related isolates

- Case –case analysis showed that certain types were statistically associated with defined exposures, for example:
  - 0129.001.002 with contact with live chickens, and working with chicken or mink farming and rural residence;
  - 0882.005.001 with contact with chickens.
  - 0083.001.002 with having a pet dog/cat; and acquisition in Nova Scotia
  - 0018.001.002 with unpasteurized milk;
  - 0926.002.001 with rural residence.
  - 0253.004.001, 0044.003.001 and 0173.002.004 with acquisition in Nova Scotia

- CGF40 increased the sensitivity of detection of outbreaks: only 4/33 temporal CGF40 clusters were identified by routine public health follow up.

- CGF40 identified outbreak cases that might otherwise be misclassified, reducing the statistical power to identify a source, e.g. 0922.001.002 3 cases identified by public health, 6 additional cases identified by typing.

- Certain types were more widely distributed and less discriminatory

- Limitations include the number of isolates not available for typing which may have reduced the ability to detect clusters or all associated isolates (see figure 1).

- Retrospective nature of study results in limited data availability

- The study isolates were predominately common species and use of this typing in less common Campylobacter spp. was not tested, although the value of typing may be negated by their rarity .

Conclusions

- CGF40 typing was validated and augmented detection of outbreaks of *Campylobacter spp*. by Public Health follow up
- Results of this study should be confirmed with prospective typing and inclusion of all isolates to allow more detailed investigation using hypothesis generating questionnaires followed by hypothesis testing.