Health Protection Scotland

NHS National Services Scotland

Quarterly report methods and caveats for the surveillance of *Clostridium difficile* infection (CDI) in Scotland

Methods

Diarrhoeal stools from patients, aged 15 and older, were tested for toxin A and B using either an immunoassay or a cytotoxicity assay. Diagnostic laboratories using the immunoassay are advised to follow a two-step diagnostic algorithm (see caveats below) jointly produced by the SSSCDRL, HPS and the Scottish Microbiology and Virology Network (SMVN). The algorithm recommends the use of a second confirmatory test following the first positive test.

A diarrhoeal stool is defined as a specimen that takes the shape of its container. A case of CDI is someone in whose stool *C. difficile* toxin has been identified at the same time as they have diarrhoea not attributable to any other cause, or from patients from whose stool *C. difficile* has been cultured at the same time as they have been diagnosed with pseudomembranous colitis (PMC).

Isolates of *C. difficile* were typed using PCR ribotyping according to the method described by O'Neill *et al.* (1996). Variable-length intragenic spacer regions of the rRNA complex were amplified by PCR, and ribotype patterns were compared directly with those of reference strains obtained from the Anaerobe Reference Laboratory (ARL) in Cardiff.

The isolates were further susceptibility tested against 9 antibiotics using Etest (AB Biodisk, Solna, Sweden). Breakpoints were derived from the Clinical and Laboratory Standards Institute (CLSI) criteria and aligned with those used in England and Wales. Antibiotics tested included: cefotaxime (64µg/ml), ciprofloxacin (≥8µg/ml), clindamycin (≥8µg/ml), erythromycin ≥8(µg/ml), levofloxacin ≥8(µg/ml), meropenem (≥16µg/ml), metronidazole ≥32(µg/ml), moxifloxacin (≥8µg/ml), piperacillin -tazobactam (≥128µg/ml), and vancomycin (≥16µg/ml).

Reporting

Incidence rates of CDI are presented by NHS board. Each case is allocated to an NHS board based on the location of the diagnostic laboratory where the specimen was tested. The surveillance does not distinguish between cases from acute, non-acute hospitals, and the community (all cases are included in the numerator). It is currently assumed that all cases have been in contact with the healthcare system and therefore can be classified healthcare associated cases. Duplicates have been removed. If a case is diagnosed twice within a 28-day period the second toxin positive test will be considered a duplicate. Following introduction of the new testing algorithm any results reported to HPS as equivocal (second test is negative following a positive first test) are removed from the final data published.

The exact date of onset of illness is not reported: instead, the **date of collecting specimen** from the patient is taken as a proxy for the onset of illness for the ECOSS reports. When this date is not available the date of receiving the specimen or date of reporting is used. Before entering the data into the dataset each diagnostic laboratory has the opportunity to review their own data.

Data analysis

Calculation of rates

The incidence rate of CDI per NHS board area for patients aged ≥65 was calculated as follows:

$$\text{Rate per 100 000 total occupied bed days} = \frac{\text{number of CDI cases} * 100\,000}{\text{OCBDs} \geq 65 \text{ in board area}}$$

The denominator for patients aged ≥65 (total occupied bed days (OCBDs)) includes patients in acute hospitals and patients in non-acute geriatric long-term stay wards except for psychiatry and obstetrics. Non-acute denominator figures have been revised (October 2006 to March 2013):

http://www.hps.scot.nhs.uk/documents/ewr/pdf2013/1336.pdf

Acute rates are not calculated separately for those aged ≥65, as these rates were found to be unsuitable for monitoring CDI in Scotland. Note that NHS Orkney does not provide a non-acute (overnight) specialty in elderly care.

The incidence rate of CDI per NHS board area for patients aged 15-64 was calculated as follows:

$$\text{Rate per 100 000 acute occupied bed days} = \frac{\text{number of CDI cases} * 100\,000}{\text{OBDs 15-64 in board area}}$$

The denominator for patients aged 15-64 (acute occupied bed days (AOBDs)) includes patients in acute hospitals only (as so few CDI patients in this age group are found in the non-acute setting).

In addition to the incidence rates per 100 000 bed days, the incidence rate of CDI was also calculated per 100 000 population for each NHS board.

Identification of outliers

Funnel plots are a type of control chart in which the observed event (in this instance rates of CDI cases) is plotted against a measure of its precision (in this case the sample size as measured by occupied bed days). The statistical analysis was based on an over-dispersed Poisson regression model with the logarithm of the occupied bed days as an offset. In the funnel plot, the incidence rates of CDI per 100 000 bed days are plotted against the number of bed days in 100 000s along with 95% confidence limits. Incidence rates outside of the 95% confidence limits are considered outliers.

Analysis of trends

Analysis of year-ending incidence rates of CDI was carried out using an over-dispersed model as above, including terms for NHS board, Year and Quarter. Hypothesis tests were carried out using F tests based upon the large sample approximation to the normal distribution. The trend analysis is based upon the most recent eight quarters of data.

Trends in incidence rates of CDI over the most recent twelve quarters were analysed using Statistical Process Control (SPC) charts. Quarterly incidence rates are plotted with a 99% confidence limit (upper warning limit).

Reference

O'Neill GL, Ogunsola FT, Brazier JS and Duerden BI. Modification of a PCR ribotyping method for application as a routine typing scheme for *Clostridium difficile*. Anaerobe 1996; 2; 205-209.

Caveats

A number of important caveats associated with the data in this report must be highlighted:

(a) Regional differences in healthcare provision and the age distribution of the population are factors likely to affect the number of persons acquiring CDI in each NHS board area;
(b) Full compliance with the national surveillance protocol has been achieved gradually at different times in the NHS boards and comparison with previous data could therefore be associated with error;
(c) Previous validation studies have shown that 9-35% of reported cases have no documented symptoms – some of these cases may have been false-positive cases. Quarterly validations are carried out to ensure that, as much as possible, only cases which meet the case definition for CDI are reported;
(d) Bed day data for the incidence rate calculations are year old data and do not reflect current quarter bed data (due to the lack of complete non-acute bed day data at the time of reporting);
(e) In August 2013, incidence rates were revised for the period October 2006 to March 2013 in both age groups. Published data before this date will not be comparable with future incidence rates. Please refer to the HPS web-site for the most up-to-date data on CDI incidence rates;
(f) The quarterly data produced by HPS are based on interim data for both bed occupancy and incidence. These data are subject to revision as finalised data becomes available. Therefore there may occasionally be minor numeric discrepancies between reports, reflecting the availability of such updated data;
(g) Between Q4 2006 to Q1 2011 population rates were calculated using the mid-2005 estimated population for Scotland. From Q2 2011 onwards population rates are calculated using the most recent mid-year population estimates available;
(h) The year-ending incidence rate analysis is only based upon eight quarters of data as this enables a year on year comparison to be made without any bias associated with seasonal effects. The analysis does not cover data from 2006 as there is evidence of different patterns in rates in many boards in the early part of the surveillance and the recent year on year change is of greater interest than historical comparison. Much of the statistical significance comes from the large numbers of cases which add power to the analysis;
(i) Some samples submitted for the snapshot programme did not grow on culture or were not *C. difficile*, and some laboratories did not have any samples to send as there were no cases of CDI during the collection period or have experienced technical issues with regards the preparation of samples; therefore, there is some bias between laboratories;
(j) Case review studies carried out between 2007 and 2009 have shown that community-associated CDI varies amongst NHS boards from 0-26%;
(k) Results in the 15-64 age group should be interpreted with caution as there may be bias due to differences in patient population characteristics among boards,

and the potential for false positives to have an exaggerated effect due to the lower prevalence in this age group;

(l) The NHS Centre for Evidence-based Purchasing (CEP) has published the results of an evaluation of the performance of commercial kits for the detection of *C. difficile* toxins and highlights issues related to the sensitivity and positive predictive values of the kits. In the context of widespread testing, this has raised doubts as to the appropriateness of using single tests for toxin detection.

A questions and answers document has been drawn up by the CDI Diagnosis Working Group and adapted by HPS. The document may be accessed from:

http://www.hps.scot.nhs.uk/haiic/sshaip/guidelinedetail.aspx?id=40852

(m) The Scottish Microbiology and Virology Network (SMVN), in collaboration with the Scottish *C. difficile* Reference Laboratory and HPS, published a revised "Recommended protocol for testing for *Clostridium difficile* and subsequent culture" in December 2012. The protocol has been revised following new evidence that has evaluated diagnostic algorithms for the diagnosis of CDI. The protocol and accompanying FAQs are available from:

http://www.hps.scot.nhs.uk/haiic/sshaip/guidelinedetail.aspx?id=53536
and
http://www.hps.scot.nhs.uk/haiic/sshaip/guidelinedetail.aspx?id=53537