



Clostridium difficile Infection Underdiagnosis: A Prospective Cohort Study.

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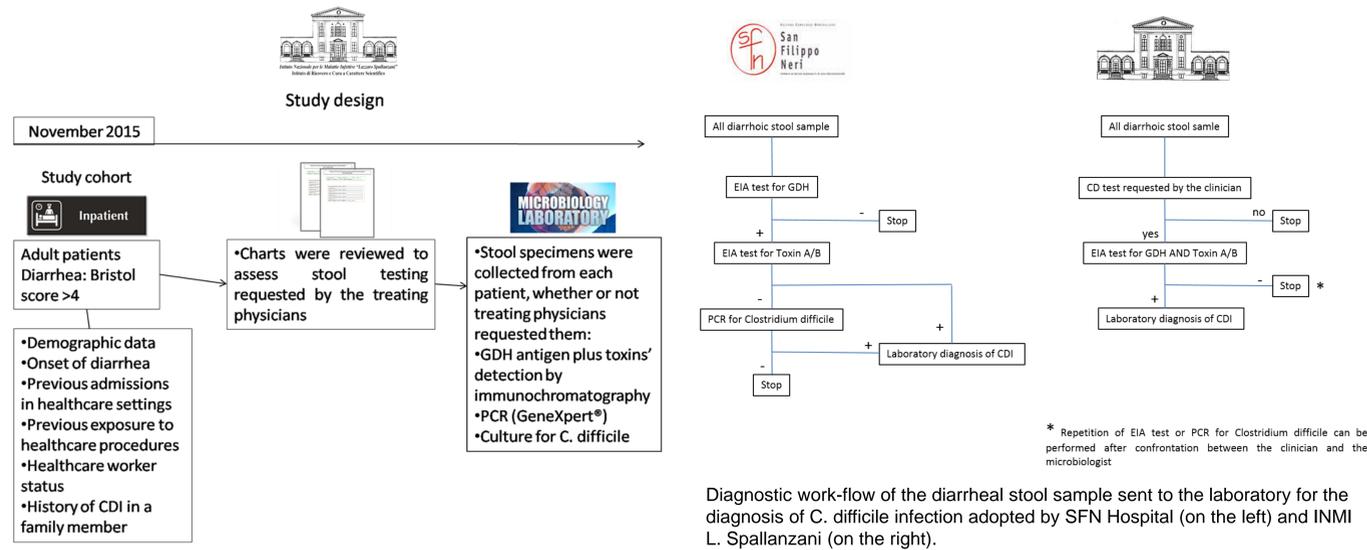
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Background:

Clostridium difficile infection (CDI) is the main cause of nosocomial infectious diarrhea. CDI underdiagnosis may delay the establishment of an anti-CDI adequate therapy leading to higher complication rates, and may contribute to increase spread within the healthcare setting. The aim of this study is to assess the burden of CDI and the rate of CDI underdiagnosis, either community- or hospital-acquired, in patients with diarrhea in two acute care hospitals.

Material and methods:

This prospective, observational study enrolled all adult patients with diarrhea in two acute care hospitals in Rome. From November 2015 to May 2018, all adult patients presenting with diarrhea at the National Institute for Infectious Diseases "L. Spallanzani" 200-bed acute care hospital were prospectively enrolled in the study. Patients enrollment was also conducted at the 400-bed acute care hospital "San Filippo Neri" from April 2017 to August 2018. Demographic data, onset of diarrhea, antibiotic administration in the previous three months, admissions in healthcare settings or exposure to healthcare procedures in the previous 3 months, healthcare worker status and history of CDI in a family member were ascertained for each patient enrolled in the study. Charts were reviewed for assessing stool testing requested by the clinicians; for each enrolled patient an additional stool sample was collected. GDH antigen plus toxins' detection by immunochromatography, PCR (GeneXpert®) were performed on each collected stool samples, whether or not requested by the clinicians.



Definitions:

- Diarrhea was defined as a stool frequency of three loose stools in 24 hours.
- Community-acquired diarrhea: onset of symptoms <48 hours from the admission in the absence of previous hospitalization, healthcare procedures in the previous 3 months, healthcare worker status.
- Community-onset healthcare-associated diarrhea: onset of symptoms <48 hours from admission in patients with the following risk factors: hospitalization/healthcare procedures in the previous 3 months, healthcare worker status.
- Hospital-acquired infections were defined as patients developing diarrhea ≥48 hours from the admission.

Definition of diagnostic CDI test result:

- Positive GDH antigen + Positive A/B toxin (EIA) or
- Positive GDH antigen, negative A/B toxin (EIA) + positive PCR analysis for TdcB or
- Positive PCR analysis for TdcB + Positive A/B toxin (EIA)

For severe and recurrent CDI, the definitions of recent European Society of Clinical Microbiology and Infectious Diseases (ESCMID) Guidelines have been used [1].

Results:

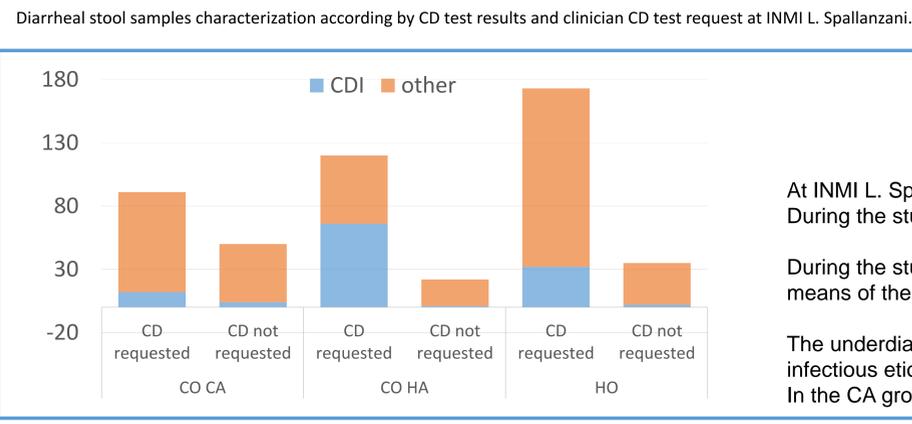
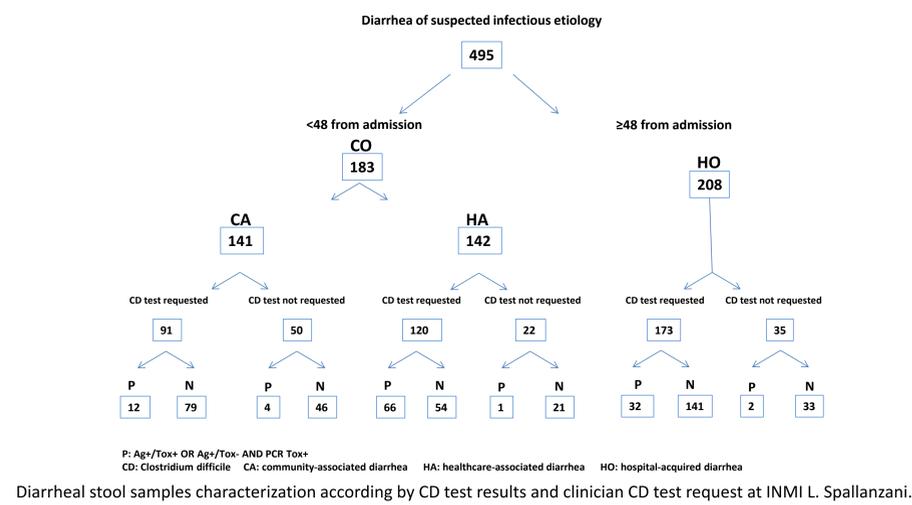
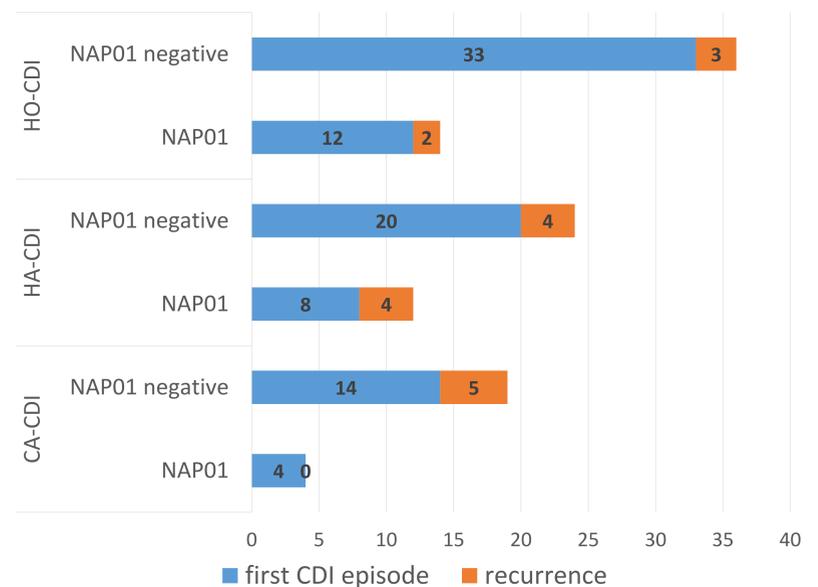
Overall, 884 patients had diarrhea during the study period and were enrolled in the study. Five hundred seventeen patients presented with diarrhea at hospital admission and 363 (41%) developed diarrhea ≥48 hours from admission. In the community-onset group, 264/517 (51.06%) and 253/517 (48.9%) presented with community- (CA) and healthcare-associated (HA) diarrhea, respectively. Overall, 231 cases of CDI (26.1%) were diagnosed in the two acute care hospitals where the study was performed.

During the study period, at INMI L. Spallanzani 7.329 patients were admitted in the hospital, 495 (6,7%) of them had diarrhea and were enrolled in the study. Two hundred eighty three (57.1%) patients presented with diarrhea at hospital admission and 208 (42.0%) developed diarrhea ≥48 hours from admission (208/7329, 2.8%). In the community-onset group, 141/283 (49.8%) and 142/283 (51.2%) presented with community- (CA) and healthcare-associated (HA) diarrhea, respectively.

Overall, 117 (23,6%) cases of CDI were diagnosed at INMI L. Spallanzani during the study. 16 CDI cases were CA, 67 HA and 34 were HO cases. In the CA group, CD test was not requested by the clinician in 50/141 (35.4%) cases. In the HA group, CD test was not requested by the clinician in 22/142 (15.4%) cases. In the nosocomial onset group (HO) CD test was not requested in 35/208 samples (16.8%). Overall, of the 107/495 (21.6%) stool samples for which CD testing was not requested, laboratory was able to detect CDI in 7 (6.5%) cases, 4 of them in the CA group, 1 in the HA group and 2 in the HO group. Regarding risk factors for CDI in the community-onset cases where CD testing was not requested, 31 were exposed to antibiotics, 1 had history of CDI in a family member.

At San Filippo Neri Hospital, 389 patients had diarrhea and were enrolled in the study. Two hundred thirty four (60.1%) patients presented with diarrhea at hospital admission and 155 (39.9%) developed diarrhea ≥48 hours from admission. In the community-onset group, 123/234 (52.5%) and 111/234 (47.4%) presented with community- (CA) and healthcare-associated (HA) diarrhea, respectively. Overall 114 cases of CDI (29.3%) were diagnosed.

In the community-onset group, 59 out of 234 (25.2%) patients were diagnosed with CDI: 23/59 (38.9%) were CA and 36/59 (61.1%) HA. In the nosocomial onset group (HO) 55/155 (35.4%) samples were CD positive.



Clinical Underdiagnosis Rate

At INMI L. Spallanzani hospital, a total of 117 CDI have been identified during the study. During the study period clinicians requested CD test on 383 out of 495 cases of diarrhea.

During the study period, a total of 110 CDI have been routinely identified by the clinicians of INMI L. Spallanzani, by means of their CD test requests to the laboratory and their confrontation with the microbiologists, when required.

The underdiagnosis rate was not negligible, and overall 1,41 CDI cases per 100 patients with diarrhea of suspected infectious etiology would have been missed. In the CA group, 2,8 CDI cases per 100 patients with diarrhea of suspected infectious etiology would have been missed.

Conclusions: During our study, CDI was diagnosed in around a fifth of patients with diarrhea of suspected infectious etiology in two large acute care hospitals settled in Rome, Italy. We diagnosed CDI in a fifth of patients with diarrhea admitted in the two hospitals, and around one fifth of them were CA. In our study, CDI underdiagnosis was not negligible; indeed, in one Hospital, in CA-diarrheas, 2,8 CDI cases per 100 patients would have been missed. Efforts should be made to optimize CDI diagnosis.