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Clostridioides difficile STRAINS EXPRESSING BINARY TOXIN ARE ASSOCIATED WITH DECREASED SUSCEPTIBILITY TO VANCOMYCIN AND METRONIDAZOLE

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Background and Aims

- *Clostridioides difficile* (*C. difficile*) infection (CDI) is the tenth leading cause of readmissions within 30 days for gastrointestinal disease and the fifth leading cause of death from nonmalignant gastrointestinal disease in the US, costing approximately US $ 4 billion[1].
- After completing initial antibiotic therapy, up to 35% of patients can have recurrent CDI. The contribution of resistance to *C. difficile*-*active antibiotics* to the outcomes of CDI is unclear.
- The aim of this study was **to evaluate the antimicrobial susceptibility of *C. difficile* isolates from patients in a US Health System and identity the bacterial and clinical variables associated with antibiotic resistance.**

Methods

- Faecal samples from adult patients with suspected CDI were collected from August 2018 to April 2019.
- *C. difficile* spores were isolated using alcohol shock and cultured in TCCFA agar plates. The presence of genes encoding *C. difficile* triose phosphate isomerase (*tpi),* toxin A (*tcdA*), toxin B (*tcdB)* and binary toxin (*cdtB)* were analyzed by qPCR.
- *C. difficile* isolates were tested for susceptibility to tigecycline (TGC), moxifloxacin (MXF), vancomycin (VAN), clindamycin (CLI), metronidazole (MTZ), and fidaxomicin (FDX) using E-test strips (Biomerieux, France, and Liofilchem, Italy), microbroth or agar dilution. The interpretation of minimum inhibitory concentration (MIC) was done according to the recommendations of CLSI M11-A7 and EUCAST.

Results

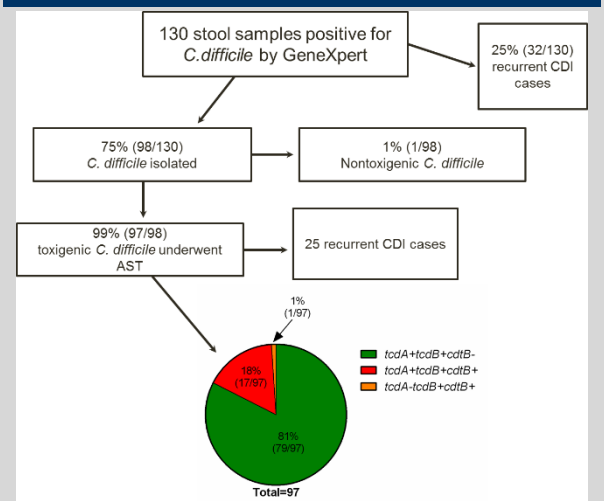

Figure 1. Study Flowchart for Clinical Specimens from Patients with *C.difficile* Infection.

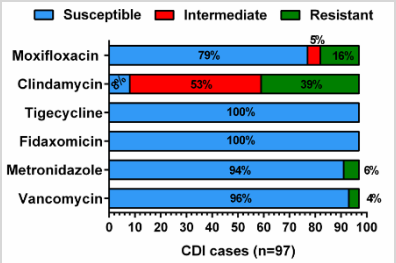

Figure 2. Antimicrobial susceptibility of *C. difficile* isolates from fecal samples of infected patients (n=97).

Among the *C. difficile* strains resistant to VAN and/or MTZ (n=6), 83% of the patients were aged with multiple comorbidities and severe CDI, as well as all the strains were binary positive (cdtB+).

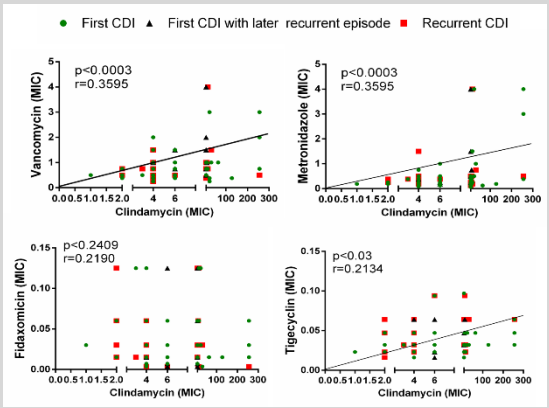

Figure 3. Correlation of clindamycin MICs with C. difficile active antibiotics (vancomycin, metronidazole, fidaxomicin, and tigecycline) among clinical isolates (Spearman rank test).

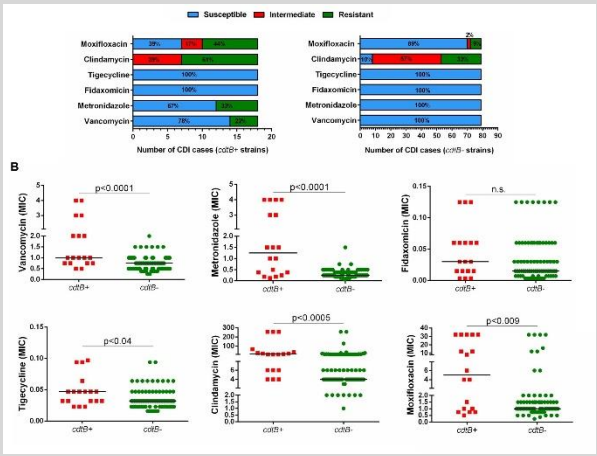

Figure 4. Antimicrobial susceptibility of *C. difficile* isolates with or without binary toxin (*cdt*).

Increased MICs did not correlate with age, disease severity or recurrent episodes presented of CDI.

Patients with chronic renal diseases (OR: 8.2, 95% CI: 2.4 to 27.6, p<0.0009) or severe disease (OR: 5.1, 95% CI: 1.5 to 17.0, p<0.007) are more likely to be infected with *cdtB*+ strains.

Conclusion

Our findings indicate that antimicrobial susceptibility of *C. difficile* to vancomycin and metronidazole is decreased in strains expressing binary toxin, which in turn is associated with severe CDI. These findings suggest the potential utility of determining binary toxin positivity in prognosis and management of CDI. Decreased antimicrobial susceptibility does not appear to increase risk of developing recurrent disease.

References

Peery AF, Crockett SD, Murphy CC, Lund JL, Dellon ES, Williams JL, Jensen ET, Shaheen NJ, Barritt AS, Lieber SR, Kochar B, Barnes EL, Fan YC, Pate V, Galanko J, Baron TH, Sandler RS. Burden and Cost of Gastrointestinal, Liver, and Pancreatic Diseases in the United States: Update 2018. Gastroenterology 2019;156(1):254-72.e11.