*Case Report*

# Clostridium difficile associated diarrhoea, successfully managed with custom prepared oral vancomycin – a Case Report

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*Sri Lankan Journal of Infectious Diseases 2022 Vol. 12(1):E13 1-5*

*DOI: http://dx.doi.org/*10.4038/sljid.v12i1.8472

## Abstract

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A 56-year-old man with multiple comorbidities presented with diarrhoea following prolonged antibiotic therapy. *Clostridium difficile* associated diarrhoea (CDAD) was confirmed by detecting *C. difficile* toxin A and B in stools with Rapid Immunoassay. The patient was managed successfully with custom prepared oral vancomycin.

***Keywords:*** *Clostridium difficile, diarrhoea, oral vancomycin, metronidazole, fidaxomicin*

## Introduction

*Clostridium difficile* associated diarrhoea (CDAD) has been poorly studied in Sri Lanka. In a previous study, Fernandopulle et al. reported that the prevalence of CDAD in a group of 32 patients who presented with acute ulcerative colitis, was 18.75% and stated that CDAD was common among Sri Lankans who presented with acute severe ulcerative colitis.[1] In contrast, Waraketiya et al. analysed stool samples of 154 patients with inflammatory bowel disease using immunoassays for *C. difficile* toxins A and B and reported that the prevalence of CDAD was as low as 0.7%.[2] In another comprehensive study of 110 patients with diarrhoea from three different tertiary care hospitals in Sri Lanka, Athukorale et al. found that the rates of CDAD were 0.01/1000 discharges, 0.008/1000 discharges and 0.004/1000 discharges respectively.[3] Collectively, these data suggest that the occurrence of CDAD in Sri Lankan patients is low compared to the numbers worldwide .

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Received 27 January 2022 and revised version accepted 4 March 2022. Published on 29.4.22

However, accurate diagnosis and prompt treatment is vital in patients with suspected CDAD in order to minimise morbidity and mortality. The treatment of choice for CDAD is fidaxomicin or oral vancomycin. Oral metronidazole is used as an alternative when the above drugs are unavailable.[4] Neither fidaxomicin nor oral vancomycin is available in Sri Lanka. Treatment failure with oral metronidazole necessitates custom preparation of oral vancomycin. There is no published data in Sri Lanka on the use of oral vancomycin in the management of CDAD patients who are unresponsive to metronidazole. This is a case report of a 56-year-old man who presented with CDAD following prolonged antibiotic therapy and was managed successfully with custom prepared oral vancomycin.

**Case presentation**

A 56-year-old man from Thabalagamuwa with a history of hypertension, ischemic heart disease, diabetes mellitus, and chronic kidney disease on regular haemodialysis was admitted with a diabetic foot infection to the District General Hospital, Trincomalee in February 2021. He was treated with intravenous ceftazidime and oral clindamycin. After 7 days, his blood culture became positive for *Candida albicans* and he was treated with intravenous fluconazole for 18 days. The patient was discharged on oral ciprofloxacin and famotidine on 11$^{th}$ March 2021.

On 18$^{th}$ March 2021, the patient was readmitted with watery diarrhoea and colicky abdominal pain. The patient was still on oral ciprofloxacin and famotidine on admission. He was haemodynamically stable with normal vital signs and had no fever. WBC was 27,800 cells/mm$^3$ with 85% neutrophils. CRP was 152mg/dl and serum creatinine was 7.5mg/dl.

The patient was referred for a microbiologist's opinion and CDAD was suspected. Treatment with oral metronidazole 600mg (three tablets of 200 mg) eight hourly with fluid therapy was commenced. He was unresponsive to oral metronidazole and diarrhoea turned into bloody loose stools with increased frequency despite seven days of metronidazole therapy. A stool sample was sent to the Medical Research Institute, Colombo for *Clostridium difficile* toxin assay. The Rapid Immunoassay of the stool sample was positive for *Clostridium difficile* toxin A and B. However, colonoscopy which showed multiple haemorrhagic patchy lesions in the sigmoid colon and rectum was inconclusive. Biopsy of the colon showed focal, mild, active inflammation of the superficial lamina propria with a few dilated and congested blood vessels.

Oral vancomycin therapy was considered, and a solution prepared following the recommended formula given in the Sanford Guide to Antimicrobial Therapy (2016).[5] Five grams of vancomycin powder was mixed with 47.5 mL sterile water containing 0.2 g saccharin, 0.05 g stevia powder, and 40 mL glycerin. Hershey's® strawberry syrup was added to constitute 100 mL that contained 50 mg vancomycin/mL in the final solution. The prepared oral vancomycin solution was refrigerated and administered orally as 2.5ml (125mg) 6 hourly. After 4 days of custom prepared oral vancomycin therapy, the patient's symptoms improved, and the diarrhoea settled. Oral vancomycin was continued for 10 days. The patient's WBC count and CRP became

normal at the time of discharge on 8th April 2021. The time line of the case report is given in figure 1.

The patient was managed with barrier nursing. Strict contact precautions were followed with hand washing and necessary PPE (gloves and gown) by the health care staff. The environment was disinfected with 1% hypochlorite solution. There were no similar cases in the ward during that period.

The timeline of the case is shown in Figure 1

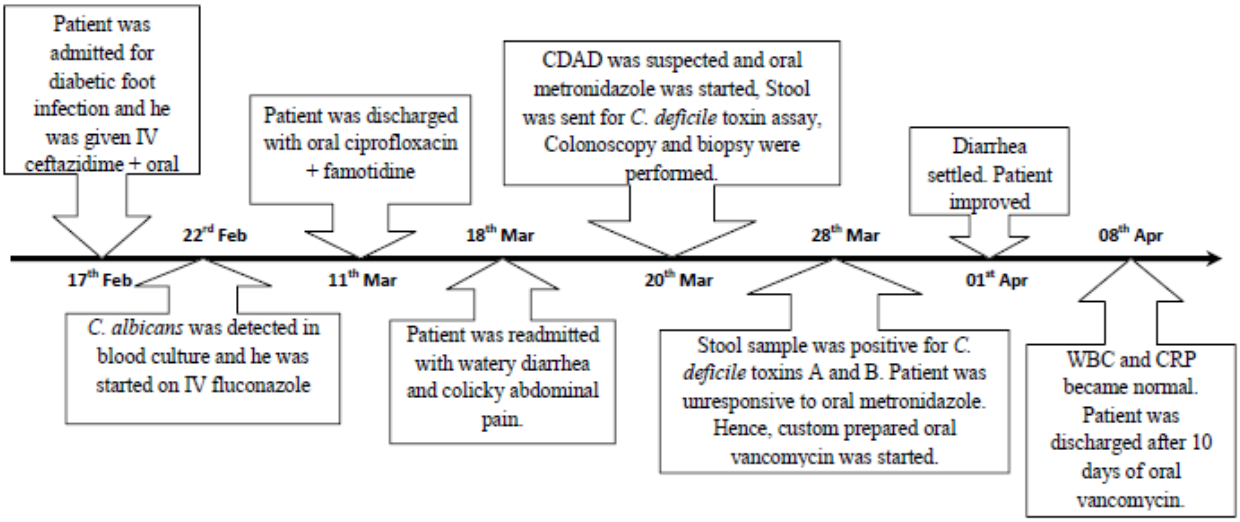


**Figure 1.** Timeline of the case

## Discussion

CDAD is defined by the presence of symptoms (usually diarrhoea) and either a stool test positive for *C. difficile* toxins or the detection of toxigenic *C. difficile*, or colonoscopic or histopathologic findings that show pseudomembranous colitis.[4] This patient was on antibiotics (third generation cephalosporin, clindamycin, ciprofloxacin and fluconazole) that are implicated in CDAD for nearly four weeks.[6] He was symptomatic, and *C. difficile* toxins A and B were present in his stools. Diabetes mellitus, chronic kidney disease and haemodialysis may have been the key contributory factors for CDAD in this patient.[6]

Oral metronidazole was begun on clinical suspicion and continued for 10 days. Both oral vancomycin and fidaxomicin were unavailable and metronidazole was available in only 200mg and 400mg tablets in Sri Lanka at the time. Dosage of metronidazole was decided as 600 mg (3 tablets of 200mg) to avoid subtherapeutic doses when parts of the tablets are given even though the recommended dosage is 500 mg.[4,5] The patient was unresponsive to oral metronidazole therapy. Poor response to oral metronidazole by CDAD patients has been reported previously too.[7] Hence, it was decided to prepare an oral vancomycin solution following the standard protocol given in the Sanford Guide to Antimicrobial Therapy (2016).[5] However, cherry syrup

was unavailable in the local market. Commercially available Hershey's® strawberry syrup was therefore substituted. This custom prepared oral vancomycin solution was helpful in managing the patient successfully.

Custom prepared oral vancomycin using the flavoured compound seems to improve patient compliance. All the ingredients for oral vancomycin solution apart from the flavouring compound were available in the hospital pharmacy. Hershey's® strawberry syrup was purchased from the local market at an affordable price. Preparation of the whole antibiotic course took about 1-2 hrs of labour time. An advantage of the recipe followed in this instance is that it allows preparation of the complete volume required for the antibiotic course rather than preparing each dose when required. Refrigeration did not seem to affect potency of the drug. However, this needs to be evaluated in the laboratory as well as clinically.

CDAD patients are to be managed ideally in isolation with strict infection control measures. As such, barrier nursing, use of PPE, contact precautions and environmental disinfection was followed by the health care staff. There is no data in Sri Lanka on cross infection with *C. difficile,* and studies on the epidemiology of *C. difficile* infections are overdue.

## Conclusion

This is the first documented case report in Sri Lanka on the management of CDAD using custom prepared oral vancomycin . Successful management of this patient required clinical awareness, availability of laboratory diagnoses and pharmaceutical knowledge, technical expertise and ingredients needed for preparation of the oral vancomycin solution.

### Declarations

Acknowledgements: We would like to acknowledge the Medical Research Institute, Colombo for *C. difficile* toxin assay
Funding source: None
Conflict of Interest statement: Authors declare no conflicts of interest
Ethics statement / Consent for publication: No personal identification is done and the reporting is based on the due treatment and care of the patient
Author contributions:
Jayatilake JAMA - Microbiological management, supervision of oral vancomycin preparation and drafting the manuscript.
Jeyalakshmy S - Patient's medical management.
Sasitharan A - Laboratory work and coordination of the management process.
Suwarnathissa PGSM - preparation of the custom made oral vancomycin.
Jayatilake JAMS - preparation and editing the manuscript.

### References

1. Fernandopulle ANR, Mayadunne PB, Navarathne NMM. The prevalence of *Clostridium difficile* infection in a cohort of Sri Lankan patients with acute severe ulcerative colitis. *Gastroenterology Hepatology Open Access* 2014; 1(2):00008. *doi: 10.15406/ghoa.2014.01.00008*

2. Waraketiya PR, de Silva AP, Wijesinghe NT, et al. *Clostridium difficile* infection in inflammatory bowel disease patients in Sri Lanka. *Sri Lanka Medical Association, 125th International Medical Congress*. 2012; 57 Supplement1:150. *No doi.*
3. Athukorala G, Fernando S, Chandrasiri N, et al. Is checking for antibiotic associated diarrhoea due to *Clostridium difficile* relevant to Sri Lankan hospitals? *Galle Medical Journal*, 2012; 17(1):5–9. *doi: http://doi.org/10.4038/gmj.v17i1.4354*
4. McDonald LC, Gerding DN, Johnson S, et al. Clinical practice guidelines for *Clostridium difficile* infection in adults and children: 2017 update by the Infectious Diseases Society of America (IDSA) and Society for Healthcare Epidemiology of America (SHEA). *Clinical Infectious Diseases* 2018; 19: 66(7):987-994. *doi: 10.1093/cid/ciy149*.
5. The Sanford Guide to Antimicrobial Therapy. Dallas, TX, USA: *Antimicrobial Therapy, Inc.*, 2016: pp 107
6. Bouza E, Burillo A, Munoz P. Antimicrobial therapy of *Clostridium difficile* associated diarrhea. *Medical Clinics of North America* 2006; 90:1141–1163. *doi: 10.1016/j.mcna.2006.07.011*
7. Musher DM, Aslam S, Logan N, et al. Relatively poor outcome after treatment of *Clostridium difficile* colitis with metronidazole. *Clinical Infectious Diseases* 2005; 40:1586–90. *doi: https://doi.org/10.1086/430311*