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Research Article

Prescribing patterns and efficacy of oral vancomycin for *Clostridium difficile* infection in Thai patients: A single center study

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ABSTRACT

Clostridium difficile infection (CDI) is a bacterial infection caused by *Clostridium difficile* (CD). The incidence and prevalence of CDI have increased, presenting a significant problem. Treatment of non-severe, initial CDI generally involves the administration of the antibiotic vancomycin as recommended by the guidelines. However, discrepancies still exist between the use of low and high dose of vancomycin in clinical practice, generating confusion for pharmacists due to the inconsistency of prescribed oral vancomycin patterns. The aim of this study was to investigate the prescribing patterns of oral vancomycin and its outcomes in adult patients diagnosed with non-severe, initial CDI. A retrospective chart review study was performed in 67 patients between January 1, 2015 and October 1, 2022. We analyzed the patterns of prescribed oral vancomycin including dose, frequency, and duration. Fisher's exact test was used to compare oral vancomycin doses and their clinical outcomes. Of the 67 patients, 44 participants met the inclusion criteria. Four prescribing patterns were discovered: 1) vancomycin 125 mg PO every 6 hours (81.8%), 2) vancomycin 250 mg PO every 6 hours (9.1%), 3) vancomycin 500 mg PO every 6 hours (2.3%), and 4) others (6.8%) (250 mg PO every 24 hours and 125 mg PO every 8 hours). The association between low and high dose of oral vancomycin and clinical outcomes was found to have no statistically significant difference (p=1.000). The results from this study could be used as fundamental information for protocol development in clinical settings.

Keywords:
Clostridium difficile, *Clostridium difficile* Infection, Vancomycin, CDI

1. INTRODUCTION

Clostridium difficile infection (CDI) is an infectious disease caused by *Clostridium difficile* (CD) bacteria, with diarrhea, pseudomembranous colitis, colonic ileus, toxic megacolon, etc. as clinical manifestations. Risk factors include broad-spectrum antibiotics (clindamycin, cephalosporins, ampicillin, and amoxycillin), chemotherapeutic drugs, gastrointestinal preparations, and acid-suppressing drugs[1-2]. The burden of CDI in the United States has been estimated at approximately 500,000 infected patients annually, with 15,000-30,000 fatalities reported[3]. In 2003, the incidence of CDI in Thailand was reported to be 18.31%[4]. The prevalence of CDI in Thailand between 2012 and 2015 was reported to be 5.68 %[5]. A recent study conducted in the northeastern region of Thailand reported the incidence rates of 0.23 cases/1,000 patient admissions and 1.78 cases/10,000 patient-days[6]. CDI is curable, but it has a high recurrence rate. The treatment of CDI depends on the patient's severity and infection episode. Antibiotic therapy is the standard treatment for CDI. The Infectious Diseases Society of America/Society for Healthcare Epidemiology of America (IDSA/SHEA) 2017 recommends either vancomycin or fidaxomicin orally for initial episode, non-severe

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CDI patients[3]. Recently, the focused update guideline for CDI prefers fidaxomicin over vancomycin for initial CDI episodes[7]. Due to the dearth of availability of fidaxomicin in Thailand, oral vancomycin is the drug of choice for non-severe CDI in the initial episode. Even though the guideline recommends a specific oral vancomycin administration regimen, we have observed controversy regarding the use in clinical practice. In the process of verifying prescriptions, the discrepancies resulting from such inconsistencies confuse physicians. Cunha et al. conducted a study to investigate the efficacy of high dose (500 mg PO every 6 hours) oral vancomycin compared with conventional dose (125-250 mg PO every 6 hours) in patients who failed after 72 hours with a conventional dose. The conclusion was that the high dose escalation of initial high dose oral vancomycin was the most efficacious regimen for *Clostridium difficile* diarrhea (CDD)[8]. Nonetheless, Chiu et al. conducted a study on the effective dose of oral vancomycin for patients with an initial episode of CDI. The results revealed that there was no significant difference in the recurrence rate between patients treated with a low dose and those treated with a high dose of oral vancomycin[9]. Due to the discrepancies in clinical practice, as well as in the literature, this study aimed to investigate prescribing patterns and explore efficacy of oral vancomycin for CDI.

2. MATERIALS AND METHODS

2.1. Study design and patients

A retrospective chart review study was conducted at Suddhavej Hospital, Faculty of Medicine, Mahasarakham University (MSU) between January 1, 2015 and October 1, 2022 to review all patient and electronic health medical records of CDI. Target sample size was 81, calculated using the Wald test comparing one proportion formula. Determined values were as follows: alpha=0.05, power=0.8, null proportion (p0)=0.8, and alternative proportion (pa)= 0.90[10]. We reported the finding in the line with Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines for observational studies[11]. Participants were included if they met the following criteria: (1) diagnosed and admitted with an initial episode of non-severe CDI (the International Classification of Diseases, Tenth Revision (ICD-10); ICD10-A04.72)), (2)≥18 years of age, and received oral vancomycin for their CDI treatments. The non-severe CDI was defined by white blood cell count (WBC) and serum creatinine (Scr); WBC<15,000 cells/mL and Scr< 1.5 mg/dL with no complications (hypotension or shock, ileus, megacolon)[3]. The CDI prescribing pattern included oral vancomycin dose, frequency of administration, and duration of therapy. The classification of low dose and high dose of oral vancomycin was as follows: 125 mg PO every 6 hours was considered a low dose regimen, while more than 125 mg PO every 6 hours was considered as a high dose. On day 3 of oral vancomycin treatment, patients showed no signs of fever or diarrhea, indicating a positive response[6]. Following the completion of a 10-day course of oral vancomycin, patients were classified as 'cured' based on the physician's judgment, provided that they remained free from fever and diarrhea.

2.2. Data collection and analysis

Data collection and extraction were performed retrospectively from medical and electronic health records. Gender, age, and comorbidity of participants were recorded. Associated information concerning risk factors associated with CDI was included; such as antibiotic usage, duration of antibiotic usage prior to the onset of diarrhea, and the use of acid-reducing medications. Clinical symptoms of CDI such as frequency of diarrhea and severity of disease were collected. This study also included duration of hospital stay, principal diagnosis of patients, type of CDI (community or hospital associated). In additional to clinical data, laboratory data (toxin A-B, WBC, Scr, and stool specimens) were included. Furthermore, this study also analyzed the patterns of prescribed oral vancomycin including dose, frequency, and duration. For categorical variables, proportions were estimated using Chi-squared or Fisher's exact test for comparisons. Quantitative variables were expressed as a mean and standard deviation (SD), and comparisons were conducted using the independent t-test after confirming normal distribution with the Shapiro-Wilk test. A *p*-value of less than 0.05 indicated statistical significance. The descriptive data analysis was performed by utilizing Statistical Package for Social Sciences (SPSS) Version 29.0 (IBM Corp.). Discrete variables were shown as cumulative frequency and relative frequency (%). Continuous variables were presented as median and range. The study protocol was approved by the Ethics Committee for Research Involving Human Subjects, MSU, Thailand (No. 002-363/ 2020).

3. RESULTS

3.1. Patient characteristics

The retrospective chart review study was performed in 67 patients who were diagnosed with non-severe, initial episode CDI from January 1, 2015 to October 1, 2022. Of the 67 patients, one patient was excluded because they were under 18 years of age. Initially, 66 underwent preliminary screening for this study. Of these, 22 participants were excluded due to incomplete medical records (n=6), changes in their final diagnosis (n=7), recipient of intravenous (IV) metronidazole and vancomycin for treatment of CDI (n=7), and recurrent CDI (n=2). Ultimately, 44 participants met the inclusion criteria for inclusion in the

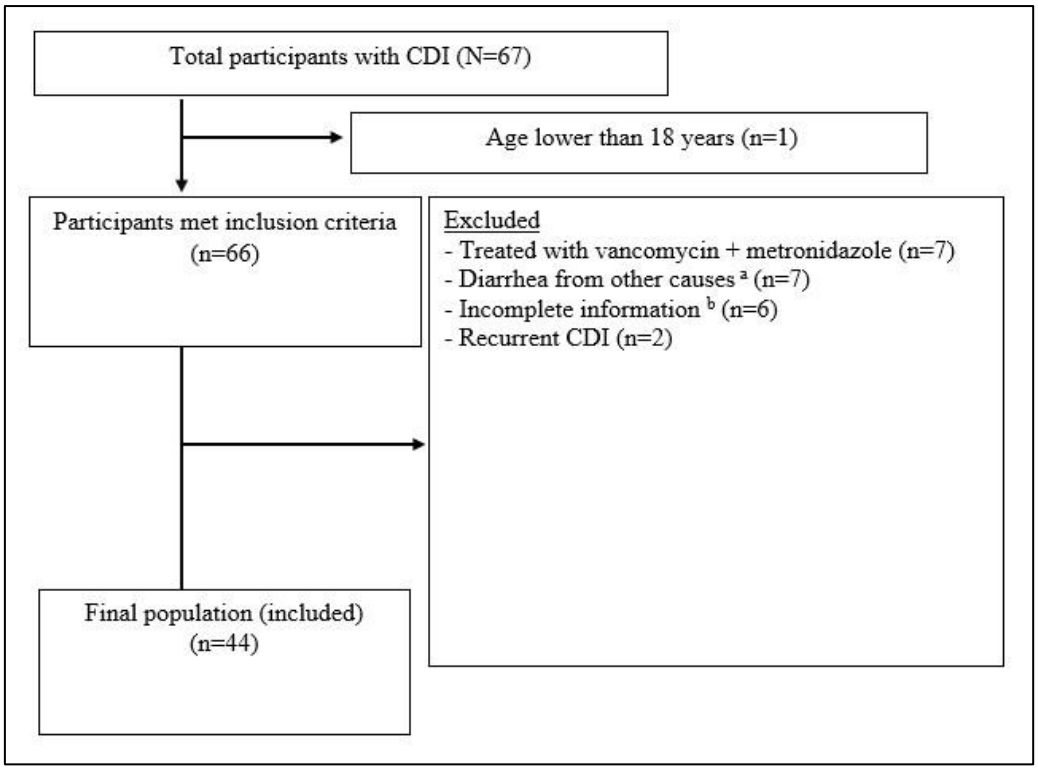

Figure 1. Describe the selection of study sample.
[a] Diarrhea from other causes was referred to non-CD bacterial infected diarrhea (n=4), non-infected diarrhea (n=2), and adverse reaction from colchicine (n=1).
[b] Incomplete information due to lack of patients' information from medical database and patient charts.

study. The flow chart for selecting study patients is shown in Figure 1.

Of the 44 included participants, males accounted for 52.3% (n=23). The average age of the participants was 65.4±19.6 years (mean±SD). The most common underlying disease among the participants was hypertension, which was present in 40.9% (n=18) of the cases. The main primary diagnosis during participants' hospital stay was infectious disease (77.3%) (n=34). Table 1 provides a detailed description of patient characteristics.

3.2. Medications associated with an increased the risk of CDI

We determined the prevalence of medications associated with an increased risk of CDI (CD-risk medications), the majority of which were antibiotics and acid-reducing agents. Our study revealed that 37 CD-risk medications were used by patients (84.0%), followed by 19 CD-risk medications that were prescribed to patients (43.1%). Meropenem accounted for 25.0% of the total, while Proton-pump inhibitors (PPIs) accounted for 54.5%. Table 2 details the frequency with which antibiotics and acid-reducing agents are used.

3.3. Prescribing patterns and clinical outcomes

There were four different prescribing patterns of oral vancomycin for non-severe, initial episode CDI identified in our study. Approximately 81% of patients were prescribed vancomycin 125 mg PO every 6 hours (low dose regimen), followed by 250 mg PO every 6 hours (high dose regimen), which was accounted for 9.1% of the total. Details of prescribing patterns are shown in Table 3. The association between low dose and high dose regimen and clinical outcomes was tested and it was demonstrated that there was no statistically significant difference (p=1.000). A detailed summary of dosage regimens is provided in Table 4.

4. DISCUSSION

The study on the utilization of oral vancomycin for non-severe, initial episode CDI revealed that vancomycin 125 mg PO every 6 hours (low dose regimen) accounted for 81.8% of treatment regimens. The average duration of therapy was 9.3±2.8 days. The administration of a low dose regimen resulted in a cure rate of 83.3% for non-severe, initial episode CDI. The results from our study demonstrated that the most frequently prescribed oral vancomycin regimen aligns closely with the IDSA/SHEA 2017 guideline[3]. However, the focused update of the recent guideline recommends fidaxomicin as a preferred regimen for initial CDI episode[7]. It is important to note that fidaxomicin is currently unavailable in Thailand. Hence, the application of this approach in clinical practice is unfeasible. In the present investigation, we have discerned the utilization of a high dose regimen, which was also

Table 1. Demographic data of included participants.

Variables	N (%)	High dose (%)	Low dose (%)	*P* value
Gender (n=44)				
Male	23 (52.30)	3 (42.90)	20 (54.10)	0.587[f]
Female	21 (47.70)	4 (57.10)	17 (45.90)	
Age (year, mean ± SD)	65.4 ± 19.6	67.0 ± 12.7	65.1 ± 20.8	0.818[g]
18-35	6 (13.60)	0 (0.00)	6 (16.20)	0.307[h]
36-50	1 (2.30)	1 (14.29)	0 (0.00)	
51-65	11 (25.00)	2 (28.57)	9 (24.30)	
66-80	17 (38.60)	3 (42.90)	14 (37.80)	
> 81	9 (20.50)	1 (14.30)	8 (21.60)	
Underlying disease[a]				
Hypertension	18 (40.90)	3 (42.90)	15 (40.50)	0.909[f]
Diabetes mellitus	16 (36.40)	2 (28.60)	14 (37.80)	0.640[f]
Chronic kidney disease	14 (31.80)	3 (42.90)	11 (29.70)	0.494[f]
Cancer	13 (29.50)	2 (28.60)	11 (29.70)	0.951[f]
Cardiovascular disease	7 (15.90)	1 (14.30)	6 (16.20)	0.898[f]
No underlying disease	2 (4.50)	1 (14.30)	1 (2.70)	0.177[f]
Auto-immune disease	1 (2.30)	0 (0.00)	1 (2.70)	1.000[h]
AIDS	1 (2.30)	0 (0.00)	1 (2.70)	1.000[h]
Gastrointestinal disease	1 (2.30)	0 (0.00)	1 (2.70)	1.000[h]
Others[b]	11 (25.00)	2 (28.60)	9 (24.30)	0.812[f]
Mode of acquisition[c]				
Hospital-acquired	26 (59.10)	2 (28.60)	24 (64.90)	0.073[f]
Community-acquired	18 (40.90)	5 (71.40)	13 (35.10)	
Severity[d]				
Mild to moderate	37 (84.10)	7 (100.00)	30 (81.10)	0.697[h]
Severe	5 (11.40)	0 (0.00)	5 (13.50)	
Severe complicated	2 (4.50)	0 (0.00)	2 (5.40)	
Duration of antibiotics used prior diarrhea				
Duration (day, mean±SD)	8.1 ± 12.5	3.0 ± 3.9	9.2 ± 13.5	0.076[i]
Frequency of diarrhea/day				
Diarrhea (frequency, mean±SD)	4.8 ± 2.4	5.2 ± 2.9	4.7 ± 2.4	0.706[g]
Primary diagnosis during the hospital stay[a]				
Infectious disease	34 (77.30)	7 (70.00)	27 (55.10)	N/A[j]
Others [e]	11 (25.00)	1 (10.00)	10 (20.40)	
Cardiovascular disease	6 (13.60)	1 (10.00)	5 (10.20)	
Gastrointestinal disorders	6 (13.60)	1 (10.00)	5 (10.20)	
Chronic obstructive pulmonary disease (COPD)	1 (2.30)	0 (0.00)	1 (2.00)	
Autoimmune disease	1 (2.30)	0 (0.00)	1 (2.00)	
Toxin A-B				
Not tested	22 (50.00)	3 (42.90)	19 (51.40)	0.713[h]
Negative	18 (40.90)	0 (0.00)	4 (10.80)	
Positive	4 (9.10)	4 (57.10)	14 (37.80)	

[a] One patient may have more than one underlying disease.
[b] Others included arthritis, gout, thalassemia, tuberculosis, dementia, benign prostatic hyperplasia, piriformis syndrome, status epilepticus, and psychosis.
[c] Mode of acquisition was defined by the time of admission to the presence of CID related clinical symptoms. If the time was less than 72 hours after admission; community acquired. If it was more than 72 hours; hospital acquired. This included if CID related clinical symptoms presented after discharge to with in four weeks.
[d] Severity was defined by severity definitions based on IDSA/SHEA 2017 guidelines[3].
[e] Others included tracheobronchitis, febrile neutropenia, anemia, acute kidney injury, fracture of lower limb, pneumothorax, cancer, pneumonitis, pituitary apoplexy, and herpes.
[f] Chi-square
[g] Independent t-test
[h] Fisher's exact
[i] Mann-Whitney U Test
[j] N/A statical analysis was not performed

Table 2. Describe the frequency of antibiotics and acid-reducing agents used.

CD-risk medications	Frequency (%)
Antibiotics[a,b]	
Cephalosporins	
Ceftazidime	8 (15.9)
Ceftriaxone	9 (22.7)
Carbapenems	
Meropenem	11 (25.0)
Ertapenem	1 (2.3)
Penicillins	
Piperacillin/tazobactam	8 (18.2)
Amoxicillin/clavulanate	1 (2.3)
Ampicillin	1 (2.3)
Others	
Clindamycin	5 (11.4)
Azithromycin	3 (6.8)
Colistin	3 (6.8)
Levofloxacin	2 (4.5)
Vancomycin	2 (4.5)
Trimethoprim/sulfamethoxazole	2 (4.5)
Doxycycline	1 (2.3)
Ciprofloxacin	1 (2.3)
Acid-reducing agents [c]	
PPIs	24 (54.5)
H_2-blockers[d]	1 (2.3)

[a]One patient may receive more than one medication.
[b]10 patients had not been prescribed antibiotics, two patients' data were not available.
[c]20 patients had not been prescribed acid-reducing agents.
[d]H2-blockers = Histamine type 2 receptor blockers.

Table 3. Describe prescribing patterns of oral vancomycin.

Prescribing patterns	Dosing group	Case (%) (n=44)	Treatment duration (day, mean±SD)	Outcomes (Case, %)		
				Cured	Not cured	Other*
125 mg PO every 6 hours	Low	36 (81.8)	9.3 ± 2.8	30 (83.3)	5 (13.9)	1 (2.8)
250 mg PO every 6 hours	High	4 (9.1)	7.5 ± 1.7	4 (100.0)	-	-
500 mg PO every 6 hours	High	1 (2.3)	10	1 (100.0)	-	-
125 mg PO every 8 hours	Low	1 (2.3)	10	1 (100.0)	-	-
250 mg PO every 8 hours	High	1 (2.3)	7	1 (100.0)	-	-
250 mg PO every 24 hours	Low	1 (2.3)	10	-	1 (100.0)	-

* Non-CDI related outcomes

Table 4. Describe the relationship of low and high dose and clinical outcomes.

	High dose	Low dose	*P* value
Not cured	1 (14.3)	6 (15.7)	1.000[a]
Cured	5 (83.3.7)	32 (84.1)	
Total	6 (100.0%)	38 (100.0%)	44 (100.0%)

[a] Fisher's exact

reported in other studies[6,8-9]. One study has reported that the administration of a high dose regimen resulted in a decrease in the number of watery stools per day compared to a low dose regimen[8]. In contrast, several studies have reported that there was no difference between high dose and low dose oral vancomycin for CDI in terms of clinical outcomes, recurrence rates, and cure rates[12-14].

The findings of O'Donnell et al. indicated that there were no significant disparities observed in terms of 90-day recurrence of CDI, clinical failure, in-hospital mortality, and 90-day readmission rates[14]. According to O'Donnell's study, the severity of CDI can impact the prescribing decisions made by healthcare providers in relation to the CDI treatment regimen. It was observed that patients with more severe manifestations of the infection were more likely to receive a higher dosage of medication[14]. Unfortunately, our study lacked sufficient statistical power to discern significant disparities in cure rates between the low dose and high dose regimens due to the limitation of our study sample size. Despite the sample size limitation, we included all patients who were diagnosed with CDI in our study. CD-risk medications, such as antibiotics and acid-reducing agents, have the potential to contribute to treatment failure in the context

of CDI therapy[15].

In our study, antibiotics and acid-reducing agents were reported to be prescribed for participants, which may have affected the outcomes. We consider that the real-world practical data provides strength to our study, which could serve as foundational information for administrative teams and policymakers to create a standard protocol for non-severe, initial episode CDI patients. The present investigation was subject to several limitations. The retrospective study methodology employed in this research was unable to show a causal relationship and led to the presence of various missing data points, including Scr and WBC. The identification of CDI in our research was based on the assessment of clinical symptoms and physician's discretion. As a result, the A-B toxin test was conducted on 50.0% of the individuals. Furthermore, it is well-established that the use of immunosuppressants in individuals with cancer can elevate the susceptibility to CDI. However, chemotherapeutic treatment in cancer patients in this study was not able to obtained due to incomplete medication history. Consequently, the conclusions derived from our research may not comprehensively reflect the characteristics and attributes of the particular group under investigation. Further research is necessary to validate the inconsistent findings reported in existing published studies.

5. CONCLUSION

There were four patterns of prescribing oral vancomycin for non-severe, initial episode CDI in our study, which vancomycin 125 mg PO every 6 hours was the most frequently prescribed and accounted for 81.8% of the total. The relationship between low and high dose of oral vancomycin and clinical outcomes were found to have no difference.

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Conflict of interest

None to declare.

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Ethics approval

This study was reviewed and approved by the Ethics Committee for Research Involving Human Subjects, MSU, Thailand. The approval number is 002-363/2020.

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AC: Conceptualization, Writing-reviewing and editing.
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PP: Conceptualization, Methodology, Investigation, Formal analysis, Project administrator, Supervision, Validation, Visualization, Roles/Writing-original draft, Writing-reviewing and editing.

REFERENCES

1. Laksamana N JJ. Antibiotic associated diarrhea. Gastroenterol Assoc Thai. 2009;17(83):25-43.
2. Triwiroj T. *Clostridium difficile* infection and fecal microbiota transplantation. J Med Heal Sci. 2017;24(2):58-71.
3. McDonald LC, Gerding DN, Johnson S, Bakken JS, Carroll KC, Coffin SE, 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). Clin Infect Dis. 2018; 66(7):e1-48.
4. Wongwanich S, Rugdeekha S, Pongpech P, Dhiraputra C. Detection of *Clostridium difficile* toxin A and B genes from stool samples of Thai diarrheal patients by polymerase chain reaction technique. J Med Assoc Thai. 2003;86(10):970-5.
5. Wangroongsarb P, Kamthalang T, Jittaprasatsin C, Cheunban N, Sriwanthana B, Sangkitporn S. Antimicrobial susceptibility and toxin production of *Clostridium difficile* isolated from diarrheal patients during 2012-2015. J Assoc Med Sci. 2017;2(5):187-96.
6. Soontornpas C, Mootsikapun P, Soontornpas R. Medication use evaluation for *Clostridium Difficile* infection: A case of super tertiary care hospital in Northeastern Thailand. Pharm Sci Asia. 2021;48(4):381-7.
7. Johnson S, Lavergne V, Skinner AM, Gonzales-Luna AJ, Garey KW, Kelly CP, et al. Clinical practice guideline by the Infectious Diseases Society of America (IDSA) and Society for Healthcare Epidemiology of America (SHEA): 2021 focused update guidelines on management of *Clostridioides difficile* infection in adults. Clin Infect Dis. 2021;73(5):e1029-44.
8. Cunha B, Sessa J, Blum S. Enhanced efficacy of high dose oral vancomycin therapy in *Clostridium difficile* diarrhea for hospitalized adults not responsive to conventional oral vancomycin therapy: Antibiotic stewardship implications. J Clin Med. 2018;7 (4):75.
9. Chiu CY, Sarwal A, Feinstein A, Hennessey K. Effective dosage

of oral vancomycin in treatment for initial episode of *Clostridioides difficile* infection: A systematic review and meta-analysis. Antibiotics (Basel). 2019;8(4):173.
10. Koo HL, Musher DM. Clostridium difficile [document on the Internet]. Antimicrobial organization; 2014 [updated 2014; cited 2023 Oct 27]. Available from: http://www.antimicrobe.org/new/b113.asp.
11. von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: Guidelines for reporting observational studies. J Clin Epidemiol. 2008; 61(4):344-9.
12. Ereshefsky B, Jin X, Rose L, Pontiggia L, Byrne D. Comparison of high-dose versus low-dose vancomycin regimens for treatment of *Clostridium difficile* infection. Open Forum Infect Dis. 2015;2 (suppl_1):1020.
13. Hsu A, Richardson C, Kuriyama SM. 1490. Vancomycin 125 mg vs. 250 mg for the treatment of non-severe and severe *Clostridium difficile* infections. Open Forum Infect Dis. 2019;6(Suppl 2): S542-3.
14. O'Donnell JN, Novak GM, Bratek BR, Singh G, Duru OO, Mitchell CL, et al. Effect of oral vancomycin dose on outcomes in patients with *Clostridioides difficile* infection. Int J Antimicrob Agents. 2021;57(4):106311.
15. Matsumoto K, Kanazawa N, Shigemi A, Ikawa K, Morikawa N, Koriyama T, et al. Factors affecting treatment and recurrence of *Clostridium difficile* infections. Biol Pharm Bull. 2014;37(11): 1811-5.