Journal of Basic and Applied Pharmacology
Vol. 5 No.1 January - June 2025

Page: [O27-35]

Original research article

Evaluation of weight-based dosing of vancomycin in hospitalized patients at a district hospital in Nakhon Si Thammarat: a descriptive retrospective study

Thanawat Khongyot[1], Wandee Kongtape[2], Thi Chantrapat[1], Taned Jettana[1], Teerapat Majam[1*]

[1]*School of Pharmacy, Walailak University, Thasala, Nakhon Si Thammarat, 80160, Thailand*
[2]*Department of Pharmacy, Thasala Hospital, Nakhon Si Thammarat, 80160, Thailand*

Received 18 November 2024; Received in revised form 4 January 2025
Accepted 20 January 2025; Available online 14 March 2025

ABSTRACT

Vancomycin, a glycopeptide antibiotic, is widely used to treat severe gram-positive infections, particularly methicillin-resistant *Staphylococcus aureus* (MRSA). Its narrow therapeutic index and variable pharmacokinetics make dosing challenging, especially in resource-limited hospitals where therapeutic drug monitoring (TDM) is unavailable. This study evaluates the appropriateness of vancomycin dosing and factors contributing to deviations from recommended regimens.

This retrospective study was conducted at a district hospital in Nakhon Si Thammarat, Thailand, from January 2012 to August 2015. Seventy-one patients receiving vancomycin were included. Demographic, clinical, and dosing data were collected from medical records. Regimens were categorized as therapeutic, subtherapeutic, or supratherapeutic based on established guidelines. Chi-square and Fisher's exact tests assessed associations between dosing adequacy and patient characteristics.

Among 78 regimens analyzed, 55.1% achieved therapeutic levels, while 44.9% were outside the target range (16.7% subtherapeutic, 28.2% supratherapeutic). The 15–20 mg/kg/dose regimen, the most frequently used, showed significant subtherapeutic dosing (44.4%, $p < 0.05$), particularly in patients >67 kg. The 500 mg HD regimen exhibited the highest rate of supratherapeutic dosing (76.9%, $p < 0.05$), highlighting challenges in post-hemodialysis dosing. Pediatric patients on the 10–15 mg/kg/dose regimen achieved therapeutic levels in 75% of cases, though 25% had supratherapeutic levels ($p < 0.05$).

This study underscores the need for individualized vancomycin dosing, adherence to evidence-based protocols, and expanded TDM access, particularly for high-risk groups like pediatric and hemodialysis patients. Standardized guidelines and real-time monitoring could improve therapeutic outcomes and reduce toxicity risks.

***Corresponding author:** teerapat.ma@wu.ac.th
https://li01.tci-thaijo.org/index.php/JBAP

Keywords: vancomycin, therapeutic drug monitoring, dosing guidelines, hemodialysis, pediatric pharmacokinetics

1. Introduction

Vancomycin, a glycopeptide antibiotic, is widely used to treat severe gram-positive bacterial infections, particularly those caused by methicillin-resistant *Staphylococcus aureus* (MRSA) and methicillin-resistant *Staphylococcus epidermidis*.[1,2] Due to its bactericidal action through inhibition of cell wall synthesis, vancomycin remains a critical therapeutic option, especially in cases where other antibiotics fail.[3] However, the drug's narrow therapeutic index poses challenges in dosing, as the difference between effective and toxic concentrations is small, increasing the risk of adverse effects if not careful.[4-6]

The pharmacokinetics of vancomycin can vary considerably among patients, influenced by factors such as weight, renal function, and underlying health conditions.[7-9] This variability makes weight-based dosing essential to achieving therapeutic efficacy while minimizing toxicity. Inaccurate dosing can result in subtherapeutic levels, risking treatment failure, or supratherapeutic levels, leading to adverse effects such as nephrotoxicity, ototoxicity, and red man syndrome.[10-12] Therapeutic drug monitoring (TDM) ensures safe and effective dosing, targeting specific serum trough levels. However, TDM resources may not be readily available in all settings, especially in smaller hospitals.[13]

The present study was conducted at a district hospital in Nakhon Si Thammarat, where vancomycin is frequently administered to hospitalized patients with severe infections. Given the variability in patient weights and the difficulty in maintaining therapeutic levels, there is a critical need to evaluate current dosing practices and their clinical outcomes. This study aims to assess the appropriateness of weight-based dosing for vancomycin, focusing on its ability to achieve therapeutic concentrations while minimizing the risk of toxicity.

2. Materials and Methods

2.1 Study design

This study was designed as a descriptive, retrospective cohort analysis to evaluate the appropriateness and outcomes of weight-based vancomycin dosing among hospitalized patients. The research was conducted at a district hospital in Nakhon Si Thammarat, Thailand, utilizing electronic medical records from the HOSxP system to obtain comprehensive patient and dosing data from January 2012 to August 2015.

Patients were eligible for inclusion if they: (1) were hospitalized and received at least one dose of vancomycin, (2) had documented body weight and renal function (serum creatinine levels) at admission, (3) had complete treatment records, including vancomycin dosing details for the study period.

Patients were excluded if they: (1) lacked adequate documentation on dosing regimens or serum trough levels, (2) received vancomycin for less than 48 h at the time of treatment.

2.2 Data collection

Patient demographic data (age, gender, body weight), clinical parameters (serum creatinine levels for renal function), and vancomycin dosing details (dosage, administration frequency, and route) were retrieved from electronic records. Where available, therapeutic drug monitoring (TDM) results, including serum trough levels, were also collected to provide insight into dosing efficacy and safety.

2.3 Dosing evaluation

Vancomycin dosing regimens were categorized based on the guidelines and previous studies into empirical and documented therapy. Empirical therapy referred to initial dosing in cases where the infective organism was not identified, while documented therapy was tailored to confirmed pathogens. Regimens

were assessed for alignment with dosing recommendations, considering patient-specific factors such as age, weight, renal function, and clinical condition.

Empirical Therapy: for adults, empirical dosing was defined as 15-20 mg/kg/dose every 8-12 h for patients with normal renal function.[14] Pediatric dosing varied by age and weight: Neonates <7 days and <1,200 g: 15 mg/kg every 24 h. Neonates >7 days and 1,200-2,000 g: 10-15 mg/kg every 12-18 h. Neonates >7 days and >2,000 g: 10-15 mg/kg every 8-12 h. Children >1 month: 10-15 mg/kg/dose every 6 h (maximum 2 g/day).[15]

Documented Therapy: Regimens were classified based on the specific infections and recommendations. For infective endocarditis, dosing varied by pathogen and clinical condition, with adult dosing typically at 30 mg/kg/day IV divided into two doses, not exceeding 2 g/day. Pediatric dosing was 40 mg/kg/day IV in 2-3 divided doses.[16] For MRSA pneumonia and bacteremia: 15-20 mg/kg/dose every 8-12 h for 2-6 weeks, depending on severity.[2] For Clostridium difficile infections: 125 mg PO every 6 h for 10-14 days, adjusted for recurrent cases.[16,17] For diabetic foot, cellulitis, and infected wounds: 1 g IV every 12 h, often combined with other antibiotics for synergy.[14]

Renal function adjustments were incorporated: for CrCl 10-50 mL/min: 1 g every 24-96 h; for CrCl <10 mL/min: 1 g every 96-168 h. Dosing in hemodialysis patients included a loading dose of 1,000 mg/dose followed by maintenance doses of 500 mg/dose post-dialysis.[14]

Regimens were categorized in the therapeutic range: doses and intervals that adhered to the guidelines and were expected to achieve adequate serum levels. Subtherapeutic: doses or intervals fell below recommendations, risking insufficient exposure. Supratherapeutic: doses or intervals exceeded recommendations, increasing the risk of toxicity.

2.4 Outcome measures

The primary outcome was the proportion of dosing regimens achieving the targeted therapeutic range. Secondary outcomes included the identification of subtherapeutic or supratherapeutic dosing incidences and associations between dosing accuracy and patient-specific factors, such as renal function and body weight.

2.5 Statistical analysis

Data were analyzed using Microsoft Excel (version 2016) for initial data management and descriptive statistics, including means, standard deviations, frequencies, and percentages to summarize patient characteristics and dosing outcomes. Further statistical analyses were conducted using SPSS (version 23). Chi-square or Fisher's exact tests were employed in SPSS to compare dosing adequacy across distinct patient subgroups (e.g., hemodialysis vs. non-hemodialysis), allowing for a more robust categorical data analysis. A p-value of <0.05 was considered statistically significant, underscoring findings with practical implications for dosing practices.

2.6 Ethical considerations

Ethical approval was obtained from the Ethics Committee in Human Research, Walailak University, Nakhon Si Thammarat, Thailand (Approval Number: WU-EC-PC-2-081-58), and all procedures adhered to institutional and ethical guidelines for research involving human subjects.

3. Results

3.1 Demographic and characteristics of patients

This descriptive retrospective study used inpatient medical records and data from the HOSxP system at a district hospital in Nakhon Si Thammarat. In the study period from January 2012 to August 2015, 73 patients were initially identified. After applying exclusion criteria, 71 patients were included in the final analysis (Fig.1).

Seventy-one patients received vancomycin therapy, with 34 males (47.9%) and 37 females (52.1%). Among the 82 vancomycin regimens administered, most patients (46.5%) were aged 35-65 years,

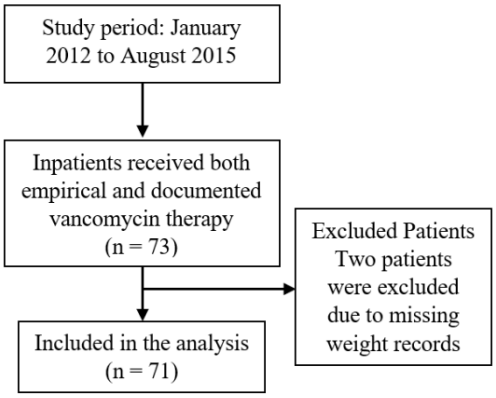

Fig. 1. Study enrolment flow chart.

followed by 31.0% who were 65 years or older. Regarding weight distribution, most patients fell within the 51-60 kg range (23.9%), followed by 61-70 kg (22.5%). The most common indication for vancomycin therapy was sepsis, accounting for 36.6% (26 cases) of all cases (Table 1).

Table 1. Demographic and characteristics of patients (n = 71).

Characteristic	N (%)
Gender	
Male	34 (47.9)
Female	37 (52.1)
Age Groups	
Newborn/Neonate (0-1 month)	5 (7.0)
Infant (1 month-1 year)	3 (4.2)
Children (1-12 years)	5 (7.0)
Adolescent (12-18 years)	0 (0.0)
Young Adult (18-35 years)	3 (4.2)
Adult (35-65 years)	33 (46.5)
Elderly (≥65 years)	22 (31.0)
Indications for Vancomycin	
Sepsis	26 (36.6)
CRBSI	7 (9.9)
Infected wound	5 (7.0)
Pneumonia	5 (7.0)
Infective endocarditis	4 (5.6)
Acute pyelonephritis	3 (4.2)
Cellulitis	3 (4.2)
Osteomyelitis	3 (4.2)
Septic shock	3 (4.2)
Infected CAPD	2 (2.8)
Respiratory distress syndrome	2 (2.8)
Febrile neutropenia	2 (2.8)

Table 1. (Cont.)

Characteristic	N (%)
Closed fracture intertrochanteric	1 (1.4)
Conjunctivitis	1 (1.4)
Diarrhea and gastroenteritis	1 (1.4)
Diabetic foot	1 (1.4)
Fever unknown origin	1 (1.4)
Meningoencephalitis	1 (1.4)
Weight Groups (kg)	
0-10	8 (11.3)
11-20	3 (4.2)
21-30	2 (2.8)
31-40	0 (0.0)
41-50	7 (9.9)
51-60	17 (23.9)
61-70	16 (22.5)
71-80	11 (15.5)
81-90	4 (5.6)
91-100	1 (1.4)
>100	2 (2.8)

Abbreviations: CRBSI, Catheter-related bloodstream infections; CAPD, continuous ambulatory peritoneal dialysis

3.2 Vancomycin regimens

A total of 78 vancomycin regimens were administered. Among these, 43 regimens (55.1%) were within the therapeutic range, while 35 (44.9%) were outside. Of the regimens outside the therapeutic range, 13 regimens (16.7%) were below the therapeutic range, indicating subtherapeutic dosing, while 22 regimens (28.2%) exceeded the therapeutic range, reflecting supratherapeutic dosing (Fig.2).

The vancomycin 15-20 mg/kg/dose regimen had the highest rate of under-dosing, with 12 out of 27 cases (44.4%) being subtherapeutic. A Chi-square test revealed a statistically significant difference ($p < 0.05$) in the distribution of under-dosed instances compared to other regimens. This finding suggests variability in weight-based dosing accuracy and underscores the importance of precise weight measurements and calculations to achieve optimal therapeutic outcomes. Patients weighing 50-67 kg were most likely to achieve therapeutic levels, while those weighing under 50 kg were prone to overdosing, and those over 67 kg were more commonly underdosed. Shorter-than-recommended dosing intervals contributed to overdosing in heavier patients.

The 1,000 mg fixed-dose regimen was used in 22 cases, with 16 regimens (72.7%) achieving the therapeutic range. One regimen (4.6%) was subtherapeutic, while five regimens (22.7%) were supratherapeutic. Supratherapeutic dosing in this group was attributed to shortened dosing intervals, which caused drug accumulation.

The 10-15 mg/kg/dose regimen, primarily used in pediatric patients, showed nine regimens (75%) within the therapeutic range, with no subtherapeutic cases but three (25%) supratherapeutic. Supratherapeutic dosing occurred more frequently in low-weight children, likely due to immature renal function affecting vancomycin clearance.

The vancomycin 500 mg HD regimen demonstrated a significantly higher rate of overdosing, with 10 out of 13 cases

(76.9%) exceeding the therapeutic range. Fisher's exact test, applied due to the small sample size, showed a statistically significant deviation in dosing ($p < 0.05$). This result highlights the challenges in post-hemodialysis dosing adjustments and emphasizes the need for better protocols to prevent vancomycin accumulation in hemodialysis patients (Table 2).

4. Discussion

This study highlights the challenges and variability in achieving optimal vancomycin dosing across different patient populations and dosing regimens. The findings align with prior research, including a prospective study conducted in Iranian medical schools from October 2011 to June 2012, which demonstrated similar deviations from the therapeutic range despite drug use evaluation protocols.[18] Subtherapeutic dosing, where serum levels fall below the minimum inhibitory concentration (MIC), risks treatment failure, incomplete bacterial eradication, and the development of resistance, particularly methicillin-resistant *Staphylococcus aureus* (MRSA).[15] Conversely, supratherapeutic dosing, with serum levels exceeding 15-20 µg/mL, increases the risks of nephrotoxicity and ototoxicity.[5,9]

The 15-20 mg/kg/dose regimen, the most frequently prescribed, demonstrated substantial variability in outcomes. Only 44.4% of regimens achieved therapeutic levels, 44.4% were subtherapeutic, and 11.1% were supratherapeutic. Weight played a significant role in these deviations. Patients weighing 50-67 kg were most likely to achieve therapeutic levels, while those weighing less than 50 kg were prone to overdosing, and patients over 67 kg were commonly underdosed. Shorter-than-recommended dosing intervals exacerbated overdosing in heavier patients. These findings emphasize the critical need for accurate weight-based dosing adjustments and adherence to dosing interval guidelines to maintain adequate serum levels throughout the dosage interval.

The 1,000 mg fixed-dose regimen, used predominantly in patients with renal impairment (CrCl <20 mL/min), achieved therapeutic levels in 72.7% of cases. However, 22.7% were supratherapeutic, often due to shortened dosing intervals leading to drug accumulation and toxicity. Conversely, extended dosing intervals resulted in subtherapeutic levels and reduced efficacy. These findings highlight the importance of renal function-based dosing adjustments and precise interval management.

The 10-15 mg/kg/dose regimen, primarily used in pediatric patients, demonstrated better performance, with 75% of regimens within the therapeutic range. No subtherapeutic cases were observed, but 25% were supratherapeutic, particularly in low-weight children. Immature renal function and age-related pharmacokinetics significantly influence vancomycin clearance in pediatric populations.[20] These results underscore the importance of incorporating age- and weight-specific dosing adjustments to prevent toxic drug accumulation in pediatric patients.

The 500 mg HD regimen for hemodialysis patients exhibited the highest rate of supratherapeutic dosing, with 76.9% of regimens exceeding the therapeutic range. High-flux dialysis membranes effectively clear vancomycin, necessitating precise post-dialysis dose adjustments.[21] Despite guidelines recommending 500 mg post-hemodialysis,[15] 10 out of 13 regimens administered 1,000 mg, leading to significant risks of nephrotoxicity.[5] This highlights the urgent need for stricter adherence to post-dialysis dosing protocols.

This study has several limitations. The retrospective design relied on medical records, which may have contained incomplete or missing data, particularly for patient weights and serum vancomycin levels, potentially affecting accuracy. The absence of comprehensive TDM data and variations in measurement timing limited the ability to correlate dosing with outcomes precisely. The findings at a single hospital may not be generalized to other settings or patient

populations, and small sample sizes in subgroups like pediatric and hemodialysis patients reduce statistical power. Additionally, practical constraints in dose adjustments, such as partial vial usage, may have influenced dosing accuracy.

Table 2. Vancomycin dosage regimens, deviations, and statistical analysis (N = 78 regimens).

Regimen	N	Dosage too high (%)	P-value	Dosage too low (%)	P-value
15-20 mg/kg/dose	27	3 (11.1)	$p < 0.05$**	12 (44.4)	$p < 0.05$***
1,000 mg	22	5 (22.7)		1 (4.6)	
10-15 mg/kg/dose	12	3(25.0)		0	
500 mg HD*	13	10 (76.9)		0	
500-1,000 mg	1	0		0	
1,000-2,000 mg	2	0		0	
15-30 mg/kg	1	0		0	

* HD: Post-hemodialysis dosing
** Fisher's exact test statistically significant ($p < 0.05$)
*** Chi-square test statistically significant ($p < 0.05$)

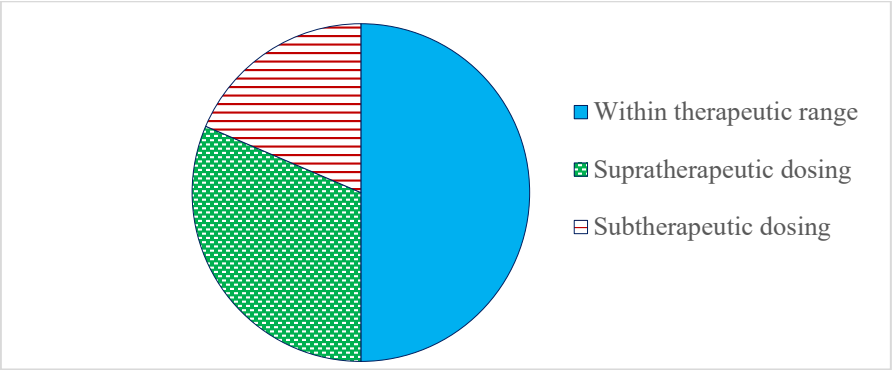

Fig.2. Distribution of vancomycin regimens by therapeutic range.

5. Conclusion

This study highlights the complexity of achieving optimal vancomycin dosing, emphasizing the significant impact of weight, renal function, and dosing intervals on therapeutic outcomes. The 15-20 mg/kg/dose regimen was associated with substantial underdosing in heavier patients. In contrast, the 500 mg HD regimen demonstrated a high rate of overdosing in hemodialysis patients, underscoring the critical need for precise post-dialysis adjustments. In pediatric patients, the 10-15 mg/kg/dose regimen showed favorable results, though supratherapeutic levels were observed in those with lower body weight due to age-related renal immaturity.

The findings underscore the necessity of individualized vancomycin dosing strategies, robust therapeutic drug monitoring, and adherence to evidence-based protocols tailored to specific patient populations. Particular attention should be given to high-risk groups, such as pediatric and hemodialysis patients, where pharmacokinetic variability is most pronounced.

Standardizing dosing guidelines and incorporating real-time monitoring can significantly reduce deviations, improve therapeutic outcomes, and mitigate the risks

of nephrotoxicity, ototoxicity, and antimicrobial resistance. Future multi-center, prospective studies are warranted to validate these findings, refine dosing practices, and ensure vancomycin's safe and effective use in diverse healthcare settings.

Acknowledgements

We thank the patients for their contribution and the authors' dedication and valuable input throughout this study.

Conflicts of interest

All authors have declared no conflict of interest.

References

[1] Gould IM, Cauda R, Wenzel RP, Grayson ML. Methicillin-resistant *Staphylococcus aureus* (MRSA): update on epidemiology, treatment options, and infection control. Curr Opin Infect Dis. 2009;22(4):338-344.

[2] Liu C, Bayer A, Cosgrove SE, Daum RS, Fridkin SK, Gorwitz RJ, et al. Clinical practice guidelines by the Infectious Diseases Society of America for the treatment of methicillin-resistant *Staphylococcus aureus* infections in adults and children: executive summary. Clin Infect Dis. 2011;52(3):285-292.

[3] Couvalin X. Mechanisms of action and resistance to glycopeptide antibiotics. Clin Microbiol Rev. 2006;19(3):493-508.

[4] Rybak MJ, Lomaestro BM, Rotschafer JC, Moellering RC Jr, Craig WA, Billeter M, et al. Vancomycin therapeutic guidelines: a summary of consensus recommendations from the Infectious Diseases Society of America, the American Society of Health-System Pharmacists, and the Society of Infectious Diseases Pharmacists. Clin Infect Dis. 2009;49(3):325-327.

[5] Marinho I, Brites MM, Gouveia T, Jorge S, Fernandes R, Lima N. Vancomycin-associated nephrotoxicity in hospitalized patients. Int J Clin Pharmacol. 2011;50(6):307-313.

[6] Black E, Lau TT, Ensom MH. Vancomycin-induced neutropenia: an overview. Can J Hosp Pharm. 2011;64(1):7-15.

[7] Elyasi S, Khalili H, Dashti-Khavidaki S, Mohammadpour A. A review of vancomycin-induced nephrotoxicity: preventive strategies. Ren Fail. 2012;34(5):608-622.

[8] Levine DP. Vancomycin: a history. Clin Infect Dis. 2006;42(1):S12.

[9] Darko W, Verdier MC, Nathanson B, Stevens W. Vancomycin-associated ototoxicity: a review. Ann Pharmacother. 2003;37(8):1024-1026.

[10] Wong-Beringer A, Joo J, Tse E, Beringer P. Risk factors and outcome of vancomycin-associated nephrotoxicity in critically ill patients. Int J Clin Pharm. 2011;33(6):596-603.

[11] Lodise TP, Lomaestro BM, Graves J, Drusano GL. Vancomycin-associated nephrotoxicity in patients with MRSA bacteremia treated in intensive care units: clinical evidence and dosing implications. Antimicrob Agents Chemother. 2008;52(4):1330-1336.

[12] Sivagnanam S, Deleu D. Red man syndrome. Crit Care. 2003;7(2):119-120.

[13] Mouton JW, Vinks AA, Punt NC. Pharmacokinetic-pharmacodynamic modeling of antimicrobial drug activity. Antimicrob Agents Chemother. 2005;49(6):2425-2431.

[14] David N, Gilbert, Henry F. Chambers, Eliopoulos GM, et al. The Sanford Guide to Antimicrobial Therapy 2014. 44th ed. Sperryville: Antimicrobial Therapy; 2014.

[15] Lv CL, Lu JJ, Chen M, Zhang R, Li QC, Chen YY, et al. Vancomycin population pharmacokinetics and dosing recommendations in haematologic malignancy with augmented renal clearance children. J Clin Pharm Ther. 2020 Dec;45(6):1278-1287.

[16] Joseph T. DiPiro, Talbert RL, Yee GC, Matzke GR, Wells BG, et al. Pharmacotherapy: a pathophysiologic approach. 9th ed. New York: McGraw-Hill Education; 2011.

[17] Cohen SH, Gerding DN, Johnson S, Kelly CP, Loo VG, McDonald LC, et al. Clinical practice guidelines for Clostridium difficile infection in adults: 2010 update by the Society for Healthcare Epidemiology of America (SHEA) and the Infectious Diseases Society of America (IDSA). Infect Control Hosp Epidemiol. 2010 May;31(5):431-55.

[18] Mahi-Birjand M, Ziaee M, Bijari B, Khalvati R, Abedini MR, Mousavi HG, et al. Evaluation of vancomycin use in university-affiliated hospitals in Southern Khorasan Province (East Iran) based on HICPAC guidelines. Drug Healthc Patient Saf. 2019 Apr 8;11:29-35.

[19] Broome CV, So CA. Consequences of suboptimal antibiotic dosing on bacterial resistance. Clin Infect Dis. 2011;53(1):S61.
[20] Pacifici GM, Allegaert K. Clinical pharmacology of vancomycin in neonates and infants: a review. Paediatr Drugs. 2012; 14(2):125-134.
[21] Launay-Vacher V, Izzedine H, Mercadal L, Deray G. Clinical review: use of vancomycin in patients undergoing dialysis. Clin Pharmacol. 2002;57(1):110-121.