

## Original Research Article

# Drug use evaluation of vancomycin at medical ward of Yekatit 12, hospital medical college, Addis Ababa, Ethiopia, 2018

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## ABSTRACT

**Background:** Drug use evaluation is an ongoing systematic process designed to maintain the appropriate medication during & after dispensing in order to assure appropriate therapeutic decision making and positive patient outcome.

**Methods:** An institutional based cross-sectional study design was conducted to analyze drug use of vancomycin by using medication charts and medical note of patients that were admitted in the medical ward of Yekatit 12 Hospital Medical College. Data was analyzed using SPSS version 20. Patients who were admitted from medical ward and whose age were  $\geq 18$  years were eligible provided that they take Vancomycin during the study period were included and Patients with medical records of insufficient or illegible information's were excluded. Structured check list was used for data collection, and the sample size was 169. Convenience sampling technique was used.

**Results:** Among 169 patients 136 (80.5%) had empiric treatments, the remaining 33 (19.5%) had specific treatments. Among 169 patients 61 (36.1%) had Infection during his/her stay in hospital of which 47 (77%) were hospital acquired pneumonia, 169 patients 39 (23.08%) had Vancomycin indication for hospital acquired pneumonia followed by 21 (12.4%), 21 (12.4%), meningitis and PCP respectively. The finding indicated that only 135 (79.9%) were appropriate regarding frequency, 124 (73.4%) were appropriate regarding dose, 104 (61.6%) were appropriate regarding duration, and the appropriate indication were only 128 (75.7%).

**Conclusions:** Vancomycine was mostly indicated as empiric therapy and only 135 (79.9%) were appropriately prescribed with respect to frequency, 128 (75.7%) were appropriate regarding indication and 124 (73.4%) were appropriate regarding to dose, 104 (61.6%) were appropriate regarding to duration. All physicians should prescribe drugs according to the guidelines.

**Keywords:** Vancomycin, Drug use evaluation, Antibiotics, Empiric therapy, Ethiopia

## INTRODUCTION

Drugs are among the most expensive input of the health service and should be used appropriately, safely and only when needed. Good drug use management is compulsory in health care system as drugs are the input that saves life. Yet large proportion of the population often lack essential medication. Because of its considerable impact on the quality of care and the cost of treatment, the selection of

medicine is one of the most cost-effective approaches to improve access to health care both in developing & developed countries.<sup>1</sup>

Drug use evaluation (DUE) is an ongoing systematic process designed to maintain the appropriate medication during & after dispensing in order to assure appropriate therapeutic decision making & positive patient outcome.<sup>2</sup>

DUE can assess the actual process of administration or dispensing of a medication (including appropriate indications, drug selection, dose, route of administration (ROA), duration of treatment & drug interaction). And also the outcome of treatment (eg. cured disease conditions or decreased levels of clinical parameter). Vancomycin is an antibiotics used to treat a number of bacterial infections. It is recommended intravenously as a treatment for complicated skin infections, blood stream infections, endocarditis, bone and joint infections and meningitis caused by methicillin resistant *staphylococcus aureus*. Vancomycin is also recommended by mouth as a treatment of severe clostridium difficile colitis when taken by mouth, it is very poorly absorbed.<sup>3</sup>

The original indication for vancomycin was for the treatment of penicillin resistant staphylococcus aureus. The rapid development of penicillin resistance by staphylococci led to its being fast tracked for approval by food and drug administration in 1958. Eli Lilly first marketed vancomycin hydrochloride under the trade name vancomycin.<sup>4</sup>

Vancomycin is indicated for the treatment of serious life-threatening infections by gram positive bacteria unresponsive to other antibiotics.<sup>5</sup>

Vancomycin is considered a last resort medication for the treatment of septicemia and lower respiratory tract, skin, and bone infections caused by gram positive bacteria. The only approved indication for oral vancomycin therapy is in the treatment of pseudo membrane colitis, where it must be given orally to reach the site of infection in the colon. Inhaled vancomycin has also been used via nebulizer for treatment of various infections of the upper and lower respiratory tract.<sup>6</sup>

The widespread misuse, together with the emergence of antimicrobial resistance and escalating unwanted expenditures have resulted in antimicrobials being the drugs most frequently chosen for DUE projects. Currently, vancomycin is choice for most patients with known infections of MRSA or MRSE. Furthermore, the use of vancomycin for life-threatening infections caused by pneumococcal organism is recommended until the culture results are available.<sup>7</sup>

The gap in Ethiopia seeks more attention as the practice of culture and sensitivity test is poor, transmission of resistant pathogens from person to person is potential and the fact that most health facilities do not have their own guideline or adhere strictly to the national guideline. Drug has been used irrationally that reduce quality of patient care resource and cause harm to patient. Apart from selective pressure from health professionals as well as patients for overuse of the drug and failure of hospital infection control practices, the lack of appropriate feedbacks after evaluative studies are conducted is a setback for intervention.<sup>8</sup>

Therefore, the initiation of this study was important for understanding the possible gaps in vancomycin utilization of the hospital and addressing them aggressively.

Implementation of drug use evaluation program is useful to monitor in health care system. The most challenging in our world today was the development of resistance to most drugs specially antibiotic due to inappropriate use of drug which may leads treatment failure and imposable to treat infectious disease. To avoid such problem drug use evaluation was the most important.

The main purpose of the study was to assess the utilization of vancomycin with respect to dose, frequency, indication, route of administration and interaction at Yekatit 12 Hospital Medical College, to provide an over view of Vancomycin use in hospital and to promote the rational prescribing, dispensing and administration of Vancomycin thereby to reduce the emergency of antibiotic resistance. More over the study contribute in identifying medication related problem and areas of inappropriate use by that it helped in identifying areas in which further information and education might be needed by health providers.

## METHODS

### *Study area and study period*

This study was carried out at Yekatit 12 Hospital Medical College which is located in Addis Ababa, Ethiopia. The hospital is a tertiary level referral and teaching hospital which provides health care services to patients. It is serving more than 5 million people in the catchment area. A study was conduct from 01May 2018 to 30July 2018 in Yekatit 12 Hospital Medical College, A.A Ethiopia.

### *Study design*

An institutional based cross sectional study was conducted to assess the use of vancomycin in Yekatit 12 Hospital Medical College.

### *Population*

Target population were all patients who were visiting in Yekatit 12 hospital medical college were target population all were representative for all samples. Source population were medication records of patients who were hospitalized in Yekatit 12 hospital medical college during study period. Sample population were all patients who were admitted from medical ward of Yekatit 12 hospital medical college and who took vancomycin as per inclusion criteria within the specified study period.

### *Sample size determination*

Sample size was calculated by using, the following statistical formula: as the proportion (p) was patients who took vancomycin from the earlier study at TASH was

12.5% and q value was 1-p which is 87.5% and 95% confidence interval, 5% margin of error.

$$n = \frac{z(1-\frac{\alpha}{2})^2 \times p(1-p)}{d^2}$$

$$\text{sample size} = \frac{(1.96)^2 \times 0.125(1 - 0.125)}{(0.05)^2}$$

Sample size = 163

Where:

n= the desired sample size, Z(1-a)= the standard normal variable a(1-a)% confidence level and is the level of significance. At 95% confidence level, the value of this parameter is 1.96 that was used in the study; p=the positive character(expected prevalence); q=the negative character; d=the degree of accuracy (absolute precision)required, usually set at 0.05.

Therefore, the sample size of the study was 169 hospitalized patients who took vancomycin. All 169 hospitalized patients admitted to the hospital during the study period as per inclusion criteria were included in the study. All patients who came with in the study period and who meet the inclusion criteria were used as study subjects.

**Sampling technique**

Random sampling method was used to include the representative of the population.

**Study variables**

Dependent variable was drug use evaluation and independent variables were age, sex and co-prescribed drugs.

**Data collection method**

Data was collected via reviewing medication charts of patients admitted during the study period by using patient data collection checklist or format. The content of the data collection format was designed to record patient information, disease condition, admission and discharge dates.

**Data collection procedure**

A structured checklist was prepared in English. Data was collected for information on assessment, sex, age, indication, dose, frequency, duration of administration, and number of co prescribed drugs with Vancomycin.

**Data quality assurance and management**

The quality of data was controlled starting from the time of data collection and data was collected and supervised

by the principal investigator. Patients name were not included in the data collection checklist.

**Data Analysis**

The collected data were entered into SPSS version 20 percentage and frequency was used to describe socio demographic characteristics. Result of the study was presented using tables.

**Ethical Consideration**

Ethical clearance letter was obtained from Universal Medical College Research and publication office. Again this ethical request was sent to Addis Ababa Health Beuro so as to assure us to conduct the study on the listed study area.

**RESULTS**

**Socio demographic characteristics**

As depicted in Table 1, among patients 63 (37.3%) were under the age category of 36-45 followed by 27 (16%) age ranges from 26-35 and 56-65, 25 (14.8%) and 20(11.8%) ranges under the age of 46-55 and 18-25 respectively. the remaining 7 (4.1%) were under the age category of >66.

**Table 1: Socio demographic characteristics, at Yekatit 12 hospital medical college, 2018.**

Variable	Frequency	Percentage
<b>Age(n=169)</b>		
18-25	20	11.8
26-35	27	16.0
36-45	63	37.3
46-55	25	14.8
56-65	27	16.0
>66	7	4.1
<b>Sex (n=169)</b>		
Male	89	52.7
Female	80	47.3

**Diagnosis and treatment**

As shown in Table 2, among 169 patients 136 (80.5%) has empiric treatments the remaining 33 (19.5%) had specific treatments. among 169 patients, 61 (36.1%) had Infection during his/her stay in hospital of which 47 (77%) were hospital acquired pneumonia, the remaining 7 (11.5%) were pneumocystic pneumonia and aspiration pneumonia. Among 169 patients 39 (23.1%) had vancomycin indication for HAP followed by meningitis and PCP each contributing for 21 (12.4%) and 21 (12.4%) respectively. Among 169 respondents 39 (23.1%) had vancomycin indication for HAP followed by 21 (12.4%), 21 (12.4%), meningitis and PCP respectively.

**Table 2: Diagnosis and treatment at Yekatit hospital medical college, August 2018.**

Variable	Frequency	Percentage
<b>Infection (n=61)</b>		
HAP	47	77.0
PCP	7	11.5
AP	7	11.5
<b>Indication of vancomycin (n=169)</b>		
HAP	39	23.1
PCP	21	12.4
Meningitis	21	12.4
Complicated UTI	20	11.8
Sepsis	19	11.2
Pulmonary effusion	14	8.3
AP	7	4.1
AV graft infection	7	4.1
Thrombosis with venous infection	7	4.1
Acute exacerbation of bronchial asthma	7	4.1
Acute myelogenous leukaemia	7	4.1
<b>Types of therapy (n=169)</b>		
Empiric	136	80.5
Specific	33	19.5

HAP=hospital acquired pneumonia; SSI=surgical site infection; PCP= pneumocystic pneumonia; AP=aspiration pneumonia AV= arterio-ventricular graft.

### Medication therapy

As presented in Table 3, among 169 responses vancomycin were taken concurrently with 27 (16%) of ceftriaxone followed by 15 (8.9%) ceftazidime, the remaining 9 (5.3%), 8 (4.7%) 7 (4.1%), 7 (4.1%) 6 (3.6%) and 5 (3%), were cotrimoxazole, NPH, azithromycin, meropenem, prednisolone, and metronidazole, respectively. In this study common drug co prescribed with vancomycin were ceftriaxone, ceftazidime and cotrimoxazole because of hospital acquired pneumonia, septic shock and aspiration pneumonia secondary to HAP and septic shock is common indication for vancomycin use. Acute exacerbation of bronchial asthma and PCP secondary to infection were the reason for co-prescription of the drug like prednisolone (hydrocortisone) and cotrimoxazole respectively.

### Dosage and frequency of vancomycin administration

The common doses of vancomycin were 1250 mg, 0.5 g, 1 g, and 1.5 g for all types of vancomycin indications. The most frequently prescribed dose was found to be 1 g and 0.5 g with daily dosage of 1g accounts for 75.7% of the cases. Among the frequency of vancomycin administration, three times daily (TID) appeared to be the most common frequency of administration.

The finding indicates that only 135(79.9%) were appropriate regarding frequency, 128(75.7%) were appropriate regarding indication and 124(73.4%) were appropriate regarding dose, 104(61.6%) were appropriate regarding duration regarding the guideline.

**Table 3: Concurrently prescribed medication with vancomycin, at Yekatit 12 hospital medical college.**

Variables	Frequency	Percent
<b>Concurrent prescribed medications</b>		
Ceftriaxone	27	16.0
Ceftazidime	15	8.9
Cotrimoxazole	9	5.3
Dexamethasone	9	5.3
NPH	8	4.7
Lasix	8	4.7
Azithromycin	7	4.1
Felodipine	7	4.1
Meropenem	7	4.1
Phenytoin	7	4.1
Atrovastatin	7	4.1
Pyridoxine	7	4.1
Asprin	7	4.1
Prednisolone	6	3.6
Ampicillin	6	3.6
Alloprinol	6	3.6
Metronidazole	5	3.0
Hydrocortisone	4	2.4
Cefipime	4	2.4
UFH	3	1.8

**Table 4: Dosage and frequency of vancomycin administration at Yekatit12 hospital.**

Characteristics	Frequency	Percentage
<b>Dose</b>		
1 g	81	47.9
0.5 g	46	27.5
1250 mg	28	16.2
1.5 g	14	8.4
<b>Frequency of administration</b>		
TID	100	59
BID	55	33
daily	7	4
QID	7	4
<b>Appropriate frequency</b>	135	79.9
<b>Appropriate indication</b>	128	75.7
<b>Appropriate dose</b>	124	73.4
<b>Appropriate duration</b>	104	61.1

## DISCUSSION

Drug utilization and evaluation is best criteria for assessing the clinical appropriateness, cost effectiveness and effective use of a drug therapy. It is reported that the

percentage of methicillin resistant *Staphylococcus aureus* (MRSA), has increased from 35.9% to 64.4% during 1992 till 2003 in the united state hospitals and the significant and incorrect use of broad spectrum antibiotics led to this important problem.<sup>9</sup> Hence, it seems to be essential to do strategic studies such as DUE. Drug Utilization evaluation of commonly used antibiotics not only will result in improved treatment efficacy, but also in conserving cost and preventing unwanted adverse effects.<sup>10</sup> So, we select vancomycin because of its important role in treatment of MRSA infection.<sup>11</sup>

In many developing countries, the guidelines for antibacterial treatment are limited, thus increasing the inappropriate use of these agents. Antibiotics are often prescribed empirically for all types of infections, both for bacterial and viral infection, further encouraging indiscriminate use of them.<sup>12</sup>

DUE is an effective mechanism to identify individual variability in drug utilization such as antibiotics.<sup>13,14</sup> Vancomycin is an antibiotic of growing importance in the treatment of hospital acquired infections, with particular emphasis on its value in the fight against MRSA. Furthermore, vancomycin is used in the treatment of serious infections caused by susceptible organisms resistant to  $\beta$ -lactam antibiotics like MRSA or in individuals with serious allergy to penicillin. However, its usage profile must be evaluated to assure maximum benefit and minimum risk. Such studies are lacking in Ethiopia.<sup>16</sup> Thus the current study aimed to assess how vancomycin was being used in Yekatit 12 hospital medical college.<sup>15</sup>

Among 169 patients included in the current study 39 (23.1%) of them had vancomycin indication for HAP followed by 21 (12.4%), 21 (12.4%), meningitis and PCP, respectively. Among 169 patients 136 (80.5%) had empiric treatments the remaining 33 (19.5%) had specific treatments. Among 169 patients 61 (36.1%) had infection during his/her stay in hospital of which 47 (77%) were hospital acquired pneumonia, the remaining 7 (11.5%) were pneumocystic carinii pneumonia and aspiration pneumonia. A study in South Africa showed only slightly better at 18.5% but with better response to Erythromycin, clindamycin and ciprofloxacin. Cost of drugs such as vancomycin, teicoplanin and linezolid is prohibitive in a very low income country such as Zimbabwe, and relying on treatment with ever costly drugs is not a solution. Prevention and infection control must be the first line measures. Antibiotic oversight is required in Zimbabwe to protect clinicians and patients from spread of drug resistance.<sup>17</sup>

The most frequent indications to vancomycin use in this study were hospital acquired pneumonia (23.1%) followed meningitis and PCP, which respectively accounts for 12.4% of the patients. The finding of this study was same to previous study done at Tikur Ambessa, where the major use of vancomycin was for pneumonia

(54%) but the percentage was lesser with this study. Moreover, In previous studies, Febrile neutropenia and primary sepsis were the two common indications to which vancomycin were most frequently used and they accounted for 87.9% and 74.5%, respectively, of the total number of reasons for vancomycin used.<sup>18,19</sup> However in study done in Iran, Tehran vancomycin was used for pneumonia at third level.<sup>20</sup>

According to the reports made by Zeleke and Engidawork the high prevalence of vancomycin use for pneumonia is suggestive of pneumonia to be the most common hospital acquired infection in the internal medicine wards of the hospital. Similarly, in this study pneumonia could represent the most prevalent hospital acquired infection in Yekatit 12 hospital.<sup>21</sup>

Emergence of antimicrobial resistance is the result of the use, overuse and misuse of antibiotics. The increased prevalence of known resistant organisms and the emergence of newly resistant organisms have resulted in delays ineffective therapy and the length of hospitalization and have led to increased cost for patients. Hence, prudent and rational use of antibiotics has to be promoted to retard the development of resistance and extend the viability of the existing medicines, which is only possible if baseline data about antibiotic utilization is available.<sup>21</sup>

As it is indicated in the result the most commonly prescribed medication with vancomycin is ceftriaxone. Both of the drugs are broad spectrum antibiotics, their combination might further extend the antibacterial coverage and have a synergistic effect. Certain studies showed that the fixed dose combination of ceftriaxone and vancomycin might be used for different infection inform of injection.<sup>22</sup>

Other study has also confirmed that the use of beta lactam antibiotics including that of ceftriaxone can enhance the activity of vancomycin against methicillin resistant *S. aureus*.<sup>23</sup> Moreover; the addition of intravenous metronidazole to oral vancomycin is associated with improved mortality in critically ill patients with *Clostridium difficile* infection.<sup>24</sup>

Although rational use is mandatory, high prevalence of MRSA may raise the consumption of glycopeptides for empiric therapy in hospitals. 136 patients have received vancomycin for empiric therapy in this study. This finding is lower than study done in Tikur Ambessa Hospital, where all of the patients in that study received empiric treatment for suspected gram-positive infections in Hong Kong hospital. This is however superior to reported study by other researchers which exhibited a 71% empiric therapy. This higher empiric therapy of vancomycin in the present study is suggestive of high prevalence of MRSA in TASH, probably necessitated a high empiric vancomycin use and independence of

vancomycin initiation and continuation with culture results because of accessibility and quality issue.<sup>25</sup>

The results of the study indicated that 24.3% of patients received vancomycin inappropriately and 75.7% as appropriately according to the guideline. However a similar study reported higher inappropriate use vancomycin (69.9%). In a case-series study, Fahimi et al., reported that 97.7% of their study population, had inappropriate indication and dosing regimen of vancomycin and they concluded that vancomycin irrational use was high compared to other countries. Compared to the above studies the utilization of vancomycin in this study setting was better.<sup>26</sup>

The doses and duration of therapy should be carefully prescribed to avoid the occurrence of resistance in bacterial infections. In this study more than half of the study participants received doses greater or equal to 500mg doses. In other study done at Iran, 63 patients received 1g every 12 hours, 4 patients 1g every 5 to 7 days, 2 patients 500mg every 8 hours, 2 patients 500mg every 6 hours, 2 patients received 1 g every 24 hours and 2 patients regimen was different from what was mentioned in the guideline. But in this study 26.6% of the patients received doses are non-concordant with guideline. An empiric antibiotic is recommended to cover for possible MRSA infection while waiting for culture identification of the infecting organism. In this finding is also in agreement with another study done by Ayazokhoo et al. in 2013. The researchers suggested that vancomycin dosing is often empiric and without consideration of GFR or any other characterization of patients.<sup>27</sup>

It is essential to promote practical guidelines about utilizing culture and sensitivity testing when considering the use of important antibiotics such as vancomycin. Also educational programs for health care professionals regarding rational use of antibiotics can be helpful in improving antimicrobial medications utilization and monitoring.

## CONCLUSION

Vancomycine was mostly indicated as empiric therapy and only 135 (79.9%) were appropriately prescribed with respect to frequency, 128 (75.7%) were appropriate regarding indication and 124 (73.4%) were appropriate regarding to dose, 104 (61.6%) were appropriate regarding to duration. All physicians should prescribe drugs according to the guidelines.

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