

**A PROSPECTIVE OBSERVATIONAL STUDY ON UTILISATION OF VANCOMYCIN IN
PAEDIATRIC INPATIENTS IN TERTIARY CARE HOSPITAL**

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ABSTRACT

Vancomycin is a glycopeptide antibiotic used to treat number of various disease conditions (especially bacterial infections). Vancomycin is frequently inappropriately prescribed, especially as empirical treatment. It is considered appropriate for treating beta lactum resistant gram positive microorganisms, but is inappropriate for beta lactum susceptible microorganisms unless the patient is severely allergic to beta lactum antimicrobials. **Aims and Objectives:** To study the empirical use of vancomycin in hospitalized pediatric patients and to optimize the inappropriate prescribing patterns of vancomycin. **Methodology:** This prospective study was conducted over a period of 6 months in 2018 to identify the inappropriate vancomycin prescription in hospitalized pediatric patients in tertiary care hospitals. The necessary data was collected from the inpatient case notes, treatment charts, patient attendants, and nursing staff. The data was analysed based on the culture sensitivity reports, indications for vancomycin prescription, duration of therapy with vancomycin, chances for drug interactions, vancomycin dosing consideration. **Results:** In our study, it was found that out of 166 patients, 138 (83.13%) patients were treated with vancomycin empirically and in 28 (16.86%) patients vancomycin was given after specific diagnosis. **Conclusion:** Infants were mostly affected with various diseases. Therapy with vancomycin was continued even though the culture sensitivity reports did not necessitate the use of vancomycin. In such conditions therapy may be shifted to other antibiotics. In certain cases weight was not considered in vancomycin therapy. This may result in sub-optimal therapeutic outcomes or toxicity. We also found that majority of patients were treated with vancomycin empirically, even though its use was not really required.

KEYWORDS: Vancomycin, Empirical treatment, Culture sensitivity tests, Paediatrics.

INTRODUCTION

Vancomycin is a glycopeptide antibiotic that is available for clinical use more than 50 years. It serves as a primary therapy for gram positive infections caused by methicillin resistant *Staphylococcus aureus* (MRSA), methicillin resistant staphylococci and ampicillin resistant *Enterococcus* species. Vancomycin is a tricyclic glycopeptide. It inhibits the biosynthesis of peptidoglycan which is a structural cell wall polymer. The peptidoglycan layer is composed of a linear polysaccharide chain composed of alternating residues of the carbohydrates N-acetyl glucosamine (GlcNAc) and N-acetyl muramic acid (MurNAc).^[1]

INDICATIONS OF VANCOMYCIN

Vancomycin is generally indicated in patients who are at high risk of developing MRSA infections, skin and soft tissue infections, musculoskeletal infections, complicated infections such as endocarditis, meningitis, nosocomial pneumonia.

PEDIATRIC DOSING OF VANCOMYCIN

The manufacturer generally recommends an initial intravenous dose of 15mg/kg, followed by 10mg/kg every 12 hours in neonates younger than one week of age and 10mg/kg every 8 hours for infants one week to one month of age, in the presence of normal renal function. Vancomycin should be used with caution in case of renal impairment. In case of renal impairment reduced rate of drug clearance occurs, which ultimately leads to drug accumulation.^[2]

SPECTRUM OF ACTIVITY

Vancomycin is active against a large number of species of gram positive cocci and bacilli such as *Staphylococcus aureus* (including methicillin-resistant strains), *Staphylococcal epidermidis* (including multiply resistant strains), *Streptococcus pneumoniae* (including multiply resistant strains), *Streptococcus pyogenes*, *Streptococcus agalactiae*, *Streptococcus bovis*, viridians group *Streptococcus*, *enterococcus*, *Clostridium* species, diphtheroids, *Listeria monocytogenes*, *Actinomyces* species and *Lactobacillus* species.

ADVERSE DRUG REACTIONS

With the increase in vancomycin use, numerous adverse drug reactions have been reported. Red man syndrome is a typical vancomycin induced ADR. Less frequently vasculitis, anaphylaxis, ototoxicity, neutropenia, fixed drug eruptions, fever, phlebitis, nephrotoxicity, thrombocytopenia and more rarely Steven Johnson syndrome or drug rash with eosinophilia and systemic symptoms (DRESS) syndrome have been reported.^[3]

EMPIRICAL USE OF VANCOMYCIN

Empiric treatment is the treatment given without knowledge of the cause or nature of the disorder and based on experience rather than logic. Sometimes urgency duplicates empirical treatment, as when a dangerous infection by an unknown organism is treated with an antibiotic. Generally broad spectrum antibiotics are employed for empirical treatment while the results of bacterial culture and other tests are awaited. Several strategies to optimize the antibiotic use have been developed. These days vancomycin is frequently employed as empirical drug for the treatment of various infections in pediatrics. Recommendations did not specifically address pediatric patients or empirical use of vancomycin before laboratory confirmation of resistant organisms.^[4]

This study assesses vancomycin utilization at pediatric hospitals, to determine risk factors for vancomycin use and length of therapy, haematologic abnormalities due to vancomycin and to facilitate recommendations to optimize prescribing practices for vancomycin in pediatrics.

MATERIALS AND METHODS

This study was a hospital based prospective observational study carried out over a period of 6 months

Distribution According To Age Criteria

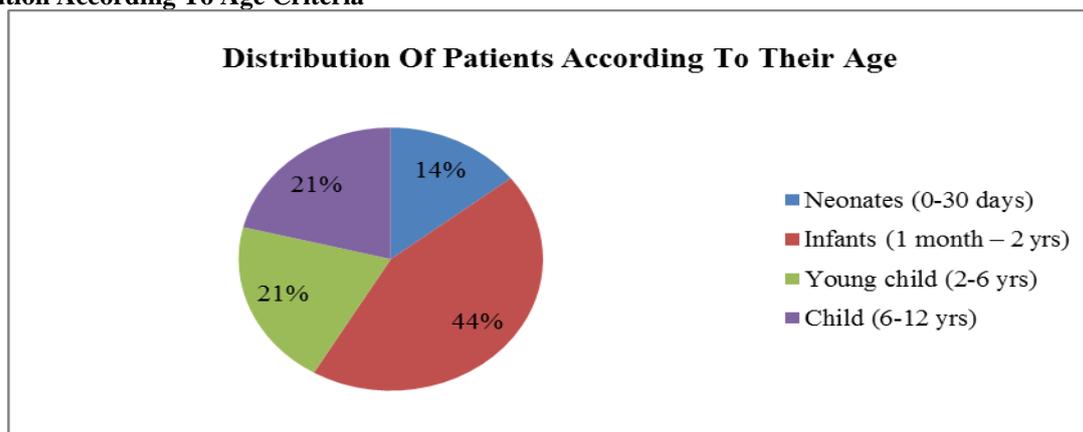


Figure 1: Graph shows age wise distribution of patients.

Distribution of Patients According To Culture Sensitivity Test Performed

Table 1: Distribution of patients according to culture sensitivity test performed.

Culture sensitivity test	Number of patients	Percentage (%)
Test performed	63	28.46
Test not performed	103	71.53

(July-December 2018) in a Tertiary Care Hospital in Karimnagar, Telangana. Patients from birth to age of 12 years, patients on treatment with vancomycin and only inpatients are included in the study. Patients who were not on vancomycin therapy and who were unconscious are excluded from the study.

Data Collection and Assessment: A suitable data collection form was designed to collect required information and analyze the data. The data collection form included the information related to patient demographics such as age, weight, along with diagnostic information (like complete blood picture, culture sensitivity results, scanning reports, renal function tests), route of administration, frequency and related information.

The analysis was done by prospective method which included the details like patients information, prescribing pattern of vancomycin, indications for vancomycin prescribing, culture reports.

Data Analysis

The data was analyzed based on information obtained from case sheets like disease conditions, culture sensitivity results in appropriate prescriptions and possible drug interactions

RESULTS

In our study a total of 166 patients were enrolled and all of them were admitted due to various disease conditions and were treated with vancomycin. Out of 166 patients, 24 were neonates, 73 were infants and young children and children were 34 and 35 respectively.

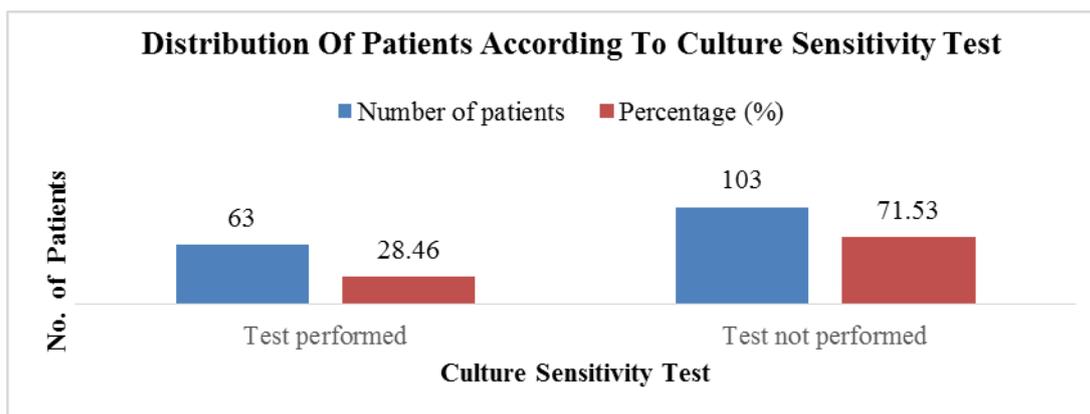


Figure 2: Graph shows distribution of patients according to culture sensitivity test performed.

Culture Sensitivity Test Results

Table 2: Culture sensitivity test results.

Results of culture sensitivity test performed	Number of patients	Percentage (%)
Culture sterile	39	61.90
Streptococcus pneumoniae	09	14.28
Hemophilus influenzae	08	12.69
Escherichia coli	07	11.11

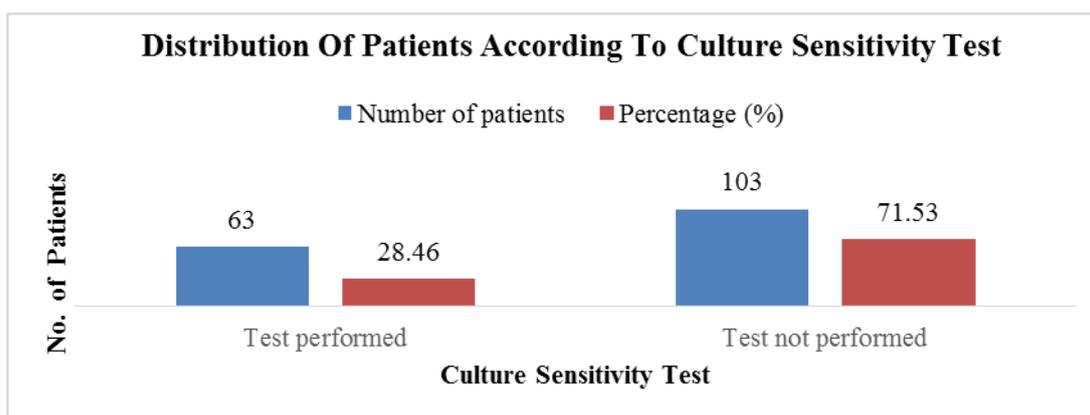


Figure 3: Pie diagram shows results of culture sensitivity tests.

Distribution of Patients According To Disease Condition

Table 3: Distribution of patients according to disease condition.

Disease condition	Number of patients	Percentage (%)
Meningitis	29	17.46
Gastroenteritis	12	7.22
Respiratory tract infection	29	17.46
Viral pyrexia	17	10.24
Seizures	19	11.44
Pancreatitis	07	4.21
Hydrocephalus	09	5.42
Abscess	08	4.81
Septic arthritis	02	1.20
Sepsis	07	4.21
Low birth weight	04	4.20
Endocarditis	04	4.20
Urinary tract infection	12	7.22
Asphyxia and tachypnoea	07	4.21

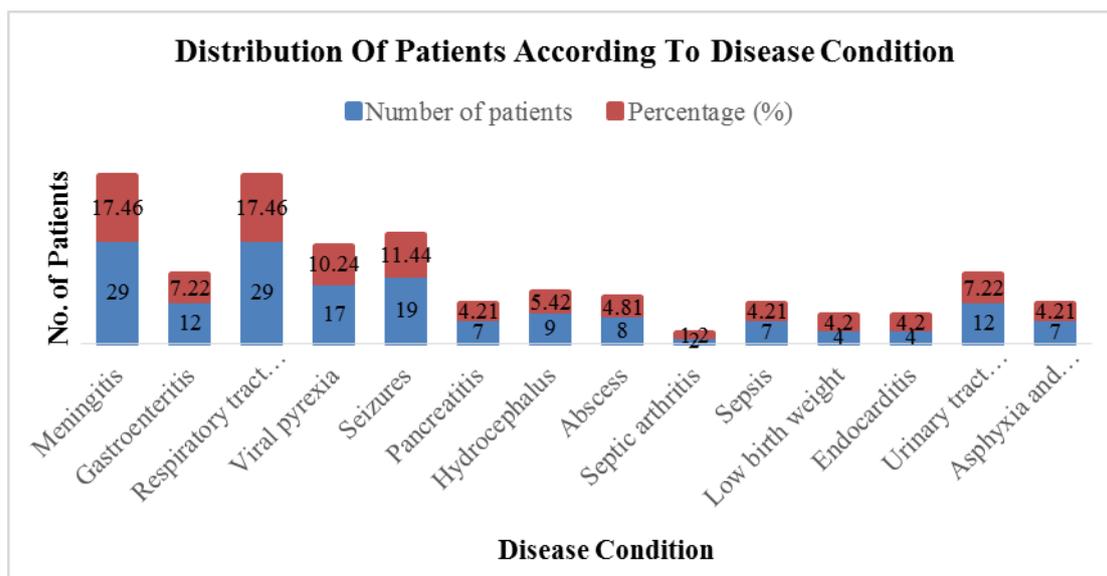


Figure 4: Graph shows distribution of patients according to disease condition.

Weight Consideration in Vancomycin Therapy

Table 4: Weight consideration in vancomycin dosing.

Weight consideration in vancomycin dosing	No. of patients	Percentage (%)
Weight considered	142	85.54%
Weight not considered	24	14.45%

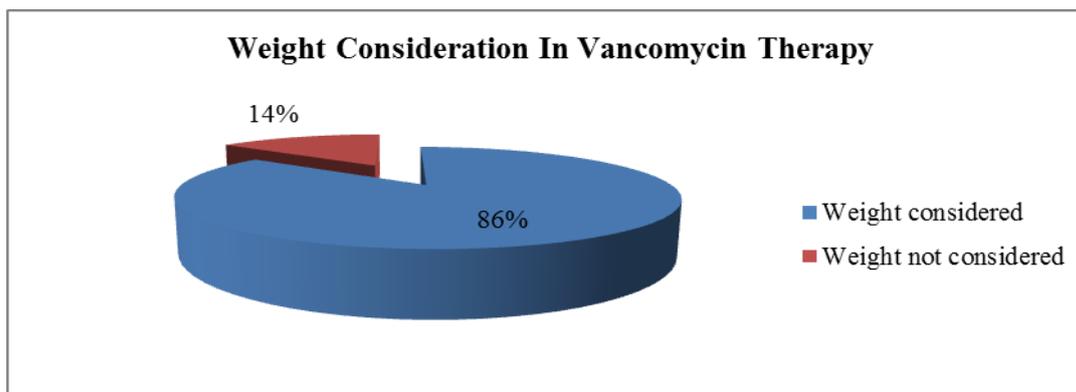


Figure 5: Graph shows weight consideration in vancomycin therapy.

Duration of Vancomycin Therapy for Various Disease Conditions

Table 5: Duration of vancomycin prescribed in various disease conditions.

Disease condition	Mean no. of days prescribed	Percentage (%)
Meningitis	7	4.21
Gastroenteritis	5	3.01
Respiratory tract infections	5	3.01
Viral pyrexia	6	3.61
Seizures	5	3.01
Pancreatitis	5	3.01
Hydrocephalus	6	3.61
Abscess	4	2.40
Asphyxia and tachypnoea	7	4.21
Septic arthritis	4	2.40
Sepsis	6	3.61
Low birth weight	3	1.80
Endocarditis	6	3.61
Urinary tract infections	5	3.01

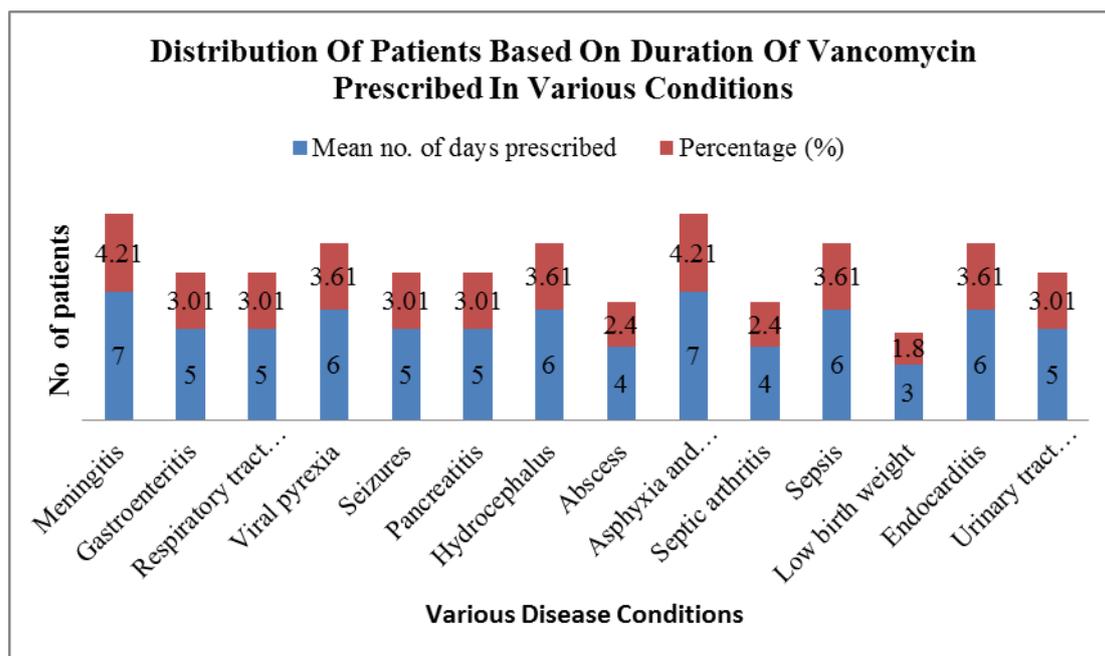


Figure 6: Graph shows duration of vancomycin prescribed in various disease conditions.

Distribution of Patients According to the use of Vancomycin

Table 6: Distribution of patients according to the use of vancomycin.

Treatment	No. of patients	Percentage (%)
Empirical therapy	138	83.13
Definitive therapy	28	16.86

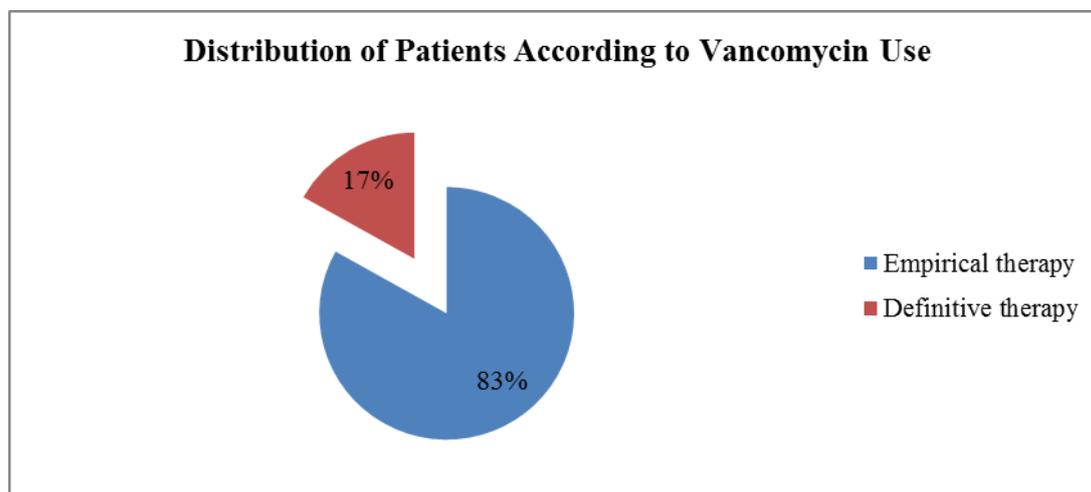


Figure 7: Graph shows distribution of patients according to the use of vancomycin.

DISCUSSION

This study is to analyze any relation between the culture sensitivity test reports and vancomycin use, risk factors for vancomycin use, duration of therapy. Reasons for choosing this project is to suggest physicians and health care providers to implement changes to improve the appropriateness of vancomycin use and to decrease the emergence of vancomycin resistant pathogens.

Harry L. Keyserling, MD*; Ronda L. Sinkowitz-Cochran conducted a study on Vancomycin use in hospitalized pediatric patients. During the study period a total of 414 cases were enrolled. The study stated that, if cultures

were negative alternative antibiotics were initiated based on culture results.^[5]

In our study, culture sensitivity test was performed in 63 patients (n=63). Out of 63 patients test results, 39 patients test result was found to be culture sterile (with a percentage of 61.90%). In 9 patients Streptococcus pneumonia was determined, followed by Haemophilus influenza in 8 patients (with a percentage of 12.29%). In 7 patients Escherichia coli was determined (with a percentage of 11.11%). Duration of therapy was not discontinued even though the test results did not necessitate the use of vancomycin.

Nak-Hyun – Kim, Hei Lim Koo *et al.* conducted a study on Inappropriate continued empirical use in a hospital with a high prevalence of Methicillin-resistant *Staphylococcus aureus*. The study stated that most frequent clinical reason for initiation of vancomycin treatment was pneumonia (90 prescriptions [18.8%]), followed by intra abdominal infections (81 prescriptions [16.9%]) and central nervous system (CNS) infections (70 prescriptions [14.6%]).^[6]

In our study, maximum use of vancomycin is seen in meningitis and respiratory tract infections and lower prevalence was observed in septic arthritis.

Harry L. Keyserling, Ronda L. Sinkowitz-Cochran conducted a study on vancomycin use in hospitalized pediatric patients. In the study, it was found that vancomycin was administered for a median of only 3 days. Length of therapy was prolonged when the illness resolved without confirmation of a microbiologic diagnosis (median 7-days) or when a therapeutic course was completed (median 9 days).

In our study, it was found that vancomycin therapy was given for about 7 days in meningitis patients and in asphyxia and tachypnoea patients. In conditions like viral pyrexia, hydrocephalus, sepsis and in endocarditis vancomycin therapy was extended for about 6 days.

In our study, we found that weight was considered in 142 patients. In remaining 28 patients weight was not considered. Weight should be considered during vancomycin dosing.

In a study, it was found that the amount of inappropriately continued empirical vancomycin treatment represented 24.9% (8.5/ 34.2 DDDs/1,000 patient-days) of the total amount of prescribed vancomycin.

In our study, it was found that out of 166 patients, 138 patients were treated with vancomycin empirically and in 28 patients vancomycin was given after proper diagnosis. It shows that majority of patients are treated with vancomycin empirically.

In the present study we found that majority of patients were infants. Duration of vancomycin varied in different disease conditions. It was given for almost 7 days in patients with meningitis and gastroenteritis and in conditions like low birth weight it administered for only 3 days. If vancomycin is used for very few days there may be chances of vancomycin resistance. In few cases weight based vancomycin dose was not considered. This may lead to sub optimal therapeutic outcomes or may even lead to toxicity.

CONCLUSION

Out of 166 patients, culture sensitivity test was performed in very few patients. Therapy with

vancomycin was continued even though the culture sensitivity reports did not necessitate the use of vancomycin. In such conditions therapy may be shifted to other antibiotics. We also found that majority of patients were treated with vancomycin empirically, even though its use was not really required.

We suggest the physicians and other health care professionals to implement changes to improve the appropriateness of vancomycin use to decrease pressures for emergence of vancomycin resistance.

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