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## A Prospective Observational Study on Dosing Accuracy of Antibiotics **Based on Creatinine Clearance in a Tertiary Care Teaching Hospital** in Kolkata



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#### ABSTRACT

Background: Antibiotics are medicines, which used to prevent and treat bacterial infections. Antibiotic resistance occurs when bacteria, viruses, fungi and parasites modify over time and not responding to medicines making infections harder for treatment and increasing the risk of spreading diseases, rigorous illness and death. Antibiotics can only treat certain kind of infections, which is caused by bacteria. The Glomerular filtration rate can determine the rate of flow of filtered fluid through kidneys. Methodology: After receiving the clearance by the Research Ethical Committee of hospital, the data was collected using suitably designed data collection form and the data was collected from patient's case file from various wards and ICU. The study was carried out for the period of 5 months. The patients were included in this study were those who had undergone through antibiotics treatment on renal impairment with all age group and sex. Result: In this study, we collected 305 patients data. These 305 patients data were reviewed throughout the study period. Renal clearance of the patients was calculated with the help of Cockcroft-Gault Formula and different standard antibiotics dosing guidelines were followed to determine the accuracy. According to this study the dosing accuracy of different antibiotics are comparatively better in ICUs than wards, among carbapenems and beta-lactum are commonly used in hospital. In carbapenems, meropenem is mostly used in hospitals.

#### **INTRODUCTION:**

Antibiotics are the medicines, which used to prevent and treat bacterial infections. Antibiotic resistance occurs when bacteria, viruses, fungi and parasites modify over time and not responding to medicines making infections harder for treatment and increasing the risk of spreading diseases, rigorous illness and death. There are many antibiotic resistance pathogens like Methicillin-Resistant *Staphylococcus aureus, Streptococcus pneumonia*, Carbapenem resistant Enterobacteriaceae. Bacteria may infect humans and animals, and the infections caused by those bacteria are difficult to treat than those caused by non-resistant bacteria.<sup>1</sup>

The prescriber who prescribes antibiotics needs to change the way it prescribes and the uses antibiotics. Although new medicines are coming back to the market, while not behavior modification, antibiotic resistance can stay a serious warning. Even if new medicines are coming to the market, without behavior change, antibiotic resistance will remain a major warning. Changes of behavior must also include actions to decrease the spread of infections through vaccination administration, hand washing, practicing safer sex, and excellent food hygiene.<sup>2</sup>

Antibiotics can only treat certain kind of infections, which is caused by bacteria. Antibiotics are also useful to treat a life-threatening condition, such as sepsis. An antibiotic does not work on viruses, such as flu, bronchitis. Antibiotics are also ineffective against some bacterial infections such as Sinus infections and ear infections. There are some common side effects of antibiotics like Rash, nausea, diarrhea, allergic reaction, and antibiotic-resistant infections.

Antibiotics play a major role in treating infections and have saved many lives. However, prescribing too many antibiotics unnecessarily can cause damage of the usefulness of these antibiotics.<sup>3</sup>

#### **Creatinine clearance**

Renal function measurement is vital for the routine care of patients. Measurement of the renal function status progression can determine the progression of kidney disease and determine the level of toxic drugs in the body. The Glomerular filtration rate can determine the rate of flow of filtered fluid through kidneys. The gold standard for the determination of GFR includes injection of inulin and its clearance through kidneys. Creatinine clearance may be defined as a volume of blood plasma cleared of creatinine per unit time.

GFR = [UrineX (mL/mg)] \* urine flow (mL/min)/ [PlasmaX (mL/mg)], where X is a substance that is completely excreted.<sup>4</sup>

**Aim& Objective-** Assessment of dosing accuracy of prescribed antibiotics based on creatinine Clarence (CrCl) level of the patients admitted in different wards and ICUs of a tertiary care teaching hospital, East India.

#### Study Criteria-

Inclusion criteria: Patients admitted in ward and intensive care unit.

Exclusion criteria: Outdoor and pediatric patients was excluded from this study.

#### **MATERIALS AND METHODS:**

After receiving the clearance by Research Ethical Committee of hospital, the data was collected using suitably designed data collection form and the data was collected from patient's case file from various wards and ICU. The study was carried out for the period of 5 months. The patients were included in this study were those who had undergone antibiotics treatment on renal impairment with all age group and sex. At first we collected patients details (Name, Age, Sex, Weight etc.)

Then we checked creatinine level in the blood of the patients and calculate the creatinine clearance (CrCl) by Cockcroft Gault equation.

 $Crcl = \{((140-age) x weight)/(72xSCr)\} x 0.85 (if female)$ 

After calculated the GFR rate of the patients, assess the accuracy of the antibiotics dosing with the recommended dose.

All collected data was transferred to Microsoft excel sheet.

#### **RESULTS AND DISCUSSION:**

#### **RESULTS:**

Data collection procedure for this research project started in April 2018 and continued till August 2018. In the whole study, 305 patients were included. Following data were obtained from the study population.

#### GENDER WISE DISTRIBUTION

**Table No. 1:** shows that total no of patients included in the study were 305 (gender wise distribution) patients. Out of which 160 were female patients (52.45%) & the remaining 145 were male patients (47.55%). Test proportion showed that proportion of female 160 (52.45%) was significantly higher than that of male145 (47.55%).

GENDER	NUMBER OF PATIENTS	PERCENTAGE
MALE	145	47.55%
FEMALE	160	52.45%
TOTAL	305	100%

#### AGE GROUP WISE DISTRIBUTION:

**Table No. 2:** shows that total no patients included in the study was 305 (age group wise distribution) patients. Out of which more than 50 age group patients were 259 (85%) & also 21-50 age group patients were 43(14.10%) rest of the patients were less than 20 patients 3. (.90%).

AGE GROUP	NO. OF PATIENTS	PERCENTAGE	
LESS THAN 20	HU3/AN	0.90%	
21-50	43	14.10%	
MORE THAN 50	259	85%	
ALL	305	100%	

#### QUINOLONES

Percentage of quinolone antibiotics used in a tertiary care teaching hospital:

21

**Table No. 3:** shows that total no of patients (QUINOLONES DERIVATIVE) used their dosing about the study was 20 (100%). 10 (50%) no of patients were used LEVOFLOXACIN & 7 (35%) no of patients were used CIPROFLOXACIN. Out of which 2 (10%) no of patients were used MOXIFLOXACIN & rest of the patient 1 (5%) was used OFLOXACIN.

DRUG NAME	NUMBER OF PATIENTS	TOTAL NO OF PATIENTS	PERCENTAGE
CIPROFLOXACIN	7		35%
MOXIFLOXACIN	2		10%
LEVOFLOXACIN	10	20	50%
OFLOXACIN	1		5%
NORFLOXACIN	0		0%



**Figure No. 1:** Graphical Representation Of Quinolone Antibiotics Used In A Tertiary Care Teaching Hospital Wise Distribution Of The Study Population:

#### CIPROFLOXACIN

#### DOSING ACCURACY WISE DISTRIBUTION

**Table No. 4:** shows that total no of patients (CIPROFLOXACIN) according to their dosing accuracy about the study were 7 (100%). Out of which 6 (86%) patients were used correct dose & rest of which 1 (14%) patients were used over dose.

DOSING ACCURACY	NO. OF PATIENTS	PERCENTAGE
Over Dose	1	14%
Under Dose	0	0%
Correct Dose	6	86%
Total Given Dose	7	100%

#### MOXIFLOXACIN

#### **DOSING ACCURACY WISE DISTRIBUTION:**

 Table No. 5: shows that total no of patients (MOXIFLOXACIN) according to their dosing accuracy was 2(100%) used correct dose.

DOSING ACCURACY	NO. OF PATIENTS	PERCENTAGE
Over Dose	0	0%
Under Dose	0	0%
Correct Dose	2	100%
Total Given Dose	2	100%

# GRAPHICAL REPRESENTATION OF DOSING ACCURACY OF MOXIFLOXACIN:

#### LEVOFLOXACIN

#### DOSING ACCURACY WISE DISTRIBUTION

**Table No. 6:** shows that total no of patients (LEVOFLOXACIN) according to their dosing accuracy about the study was 10 (100%). Out of which 6 (60%) patients were used correct dose & rest of which 4 (40%) patients were used over dose.

DOSING ACCURACY	NO. OF PATIENTS	PERCENTAGE
Over Dose	4	40%
Under Dose	0	0%
Correct Dose	6	60%
Total Given Dose	10	100%

#### **BETA-LACTUM ANTIBIOTICS**

## PERCENTAGE OF BETA-LACTUM ANTIBIOTICS USED IN A TERTIARY CARE TEACHING HOSPITAL

**Table No. 7:** shows that total no of different type of  $\beta$ -LACTUM antibiotics used in total patients were 208 (100%). Out of which, 104 (50%) patients were used MEROPENEM & 2 (1%) patients were used DORIPENEM. 57 (27%) patients were used PIPERACILLIN & TAZOBACTUM & 29 (14%) patients were used CEFUROXIME .Rest of 16 (8%)patients were used CO-AMOXICLAV.

DRUG NAME	NUMBER OF PATIENTS	TOTAL NO OF PATIENTS	PERCENTAGE
MEROPENEM	104		50%
DORIPENEM	2		1%
PTZ	57	208(100%)	27%
CO-AMOXICLAV	16		8%
CEFUROXIME	29		14%



**Figure No. 2:** Graphical Representation Of Beta-Lactum Antibiotics Used In A Tertiary Care Teaching Hospital Wise Distribution of The Study Population:

#### MEROPENEM

#### DOSING ACCURACY WISE DISTRIBUTION:

**Table No. 8:** shows that total no. of patient (MEROPENEM) according to their dosing accuracy about study was 104 (100%) out of which 78 (75%) patients were used correct dose & rest of 24 (23%) patients were used over dose. 2 (2%) patients were used underdose.

DOSING ACCURACY	NO. OF PATIENTS	PERCENTAGE
Over Dose	24	23%
Under Dose	2	2%
Correct Dose	78	75%
Total Given Dose	104	100%

#### DORIPENEM

#### DOSING ACCURACY WISE DISTRIBUTION

**Table No. 9:** shows that total no of patients (DORIPENEM) according to their dosing accuracy about the study was 2 (100%). Out of which 1 (50%) patients were used correct dose & rest of 1 (50%) patients were used overdose.

DOSING ACCURACY	NO. OF PATIENTS	PERCENTAGE
Over Dose	1	50%
Under Dose	0	0%
Correct Dose	1	50%
Total Given Dose(Pts.)	2	100%

#### PIPERACILLIN & TAZOBACTUM

#### DOSING ACCURACY WISE DISTRIBUTION

**Table No. 10:** shows that total no of patients (PIPERICILLIN & TAZOBACTUM) according to their dosing accuracy about the study was 57 (100%). Out of which 46 (81%) patients were used correct dose & 6 (10%) patients were used underdose. Rest of which 5 (9%) patients were used overdose.

DOSING ACCURACY	NO. OF PATIENTS	PERCENTAGE
Over Dose	5	9%
Under Dose	6	10%
Correct Dose	46	81%
Total Given Dose	57	100%

#### **CO-AMOXICLAV**

#### DOSING ACCURACY WISE DISTRIBUTION

**Table No. 11:** shows that total no of patients (CO-AMOXICLAV) according to their dosing accuracy about the study was 16 (100%) used in correct dose.

DOSING ACCURACY	NO. OF PATIENTS	PERCENTAGE
Over Dose	0	0%
Under Dose	0	0%
Correct Dose	16	100%
Total Given Dose	16	100%

#### CEFUROXIM

#### DOSING ACCURACY WISE DISTRIBUTION

**Table No. 12:** shows that total no of patients (CEFUROXIM) according to their dosing accuracy about the study was 29 (100%) patients used correct dose.

DOSING ACCURACY	NO. OF PATIENTS	PERCENTAGE
Over Dose	0	0%
Under Dose	0	0%
Correct Dose	29	100%
Total Given Dose	29	100%

#### AMINOGLYCOSIDE ANTIBIOTICS

## PERCENTAGE OF AMINOGLYCOSIDE ANTIBIOTICS USED IN A TERTIARY CARE TEACHING HOSPITAL

**TABLE NO. 13:** shows that total no of given dosage to patients in the study (percentage of aminoglycoside used) 8 patients were included in the study out of which 7 (87%) were used AMIKACIN & rest of patient 1 (13%) was used GENTAMYCIN.

DRUG NAME	NUMBER OF PATIENTS	TOTAL NO OF PATIENTS	PERCENTAGE
AMIKACIN	7	8	87%
GENTAMYCIN	1		13%

#### AMIKACIN

#### DOSING ACCURACY WISE DISTRIBUTION

**Table No. 14:** Total no of given (AMIKACIN) dosage according to the patients about the study (dosing accuracy wise distribution) were 7 out of which were correct dosage 6 (86%) & rest of which was under dosage 1 (14%).

DOSING ACCURACY	NO. OF PATIENTS	PERCENTAGE
Over Dose	0	0%
Under Dose	1	14%
Correct Dose	6	86%
Total Given Dose	7	100%

#### MACROLIDES

## PERCENTAGE OF MACROLIDE ANTIBIOTICS USED IN A TERTIARY CARE TEACHING HOSPITAL

**Table No. 15:** shows that total no of patients (FOSFOMYCIN) used their dosing accuracy in the study was 11 (69%). Out of which 4 (25%) patients were given AZITHROMYCIN & rest of which 1 (6%) patients were given CLARITHROMYCIN.

DRUG NAME	NUMBER OF PATIENTS	TOTAL NO OF PATIENTS	PERCENTAGE
ERYTHROMYCIN	0		0%
AZITHROMYCIN	4		25%
CLARITHROMYCIN	1	16	6%
ROXITHROMYCIN	0		0%
FOSFOMYCIN	11		69%

#### AZITHROMYCIN



**Table No. 16:** shows that total no of patients (AZITHROMYCIN) according to their dosing accuracy about the study was 4 (100%) patients used correct dose.

DOSING ACCURACY	NO. OF PATIENTS	PERCENTAGE
Over Dose	0	0%
Under Dose	0	0%
Correct Dose	4	100%
Total Given Dose	4	100%

#### FOSFOMYCIN

#### DOSING ACCURACY WISE DISTRIBUTION

**Table No. 17:** shows that total no of patients (FOSFOMYCIN) according to their dosing accuracy about the study were 11 (100%). Out of which 8 (73%) patients were used under dose & 2 (18%) patients were used correct dose. Rest of which 1 (9%) patients were used overdose.

DOSING ACCURACY	NO. OF PATIENTS	PERCENTAGE
Over Dose	1	9%
Under Dose	8	73%
Correct Dose	2	18%
Total Given Dose	11	100%

#### **GLYCOPEPTIDE ANTIBIOTICS**

#### VANCOMYCIN

#### DOSING ACCURACY WISE DISTRIBUTION

**Table No. 18:** shows that total no of given dose to patients (VANCOMYCIN) according to their dosing accuracy about the study were 10 (100%). Out of which 5 (50%) patients were used correct dose & 4 (40%) patients were used overdose & rest of the patients were used underdose.

DOSING ACCURACY	NO. OF PATIENTS	PERCENTAGE
Over Dose	4	40%
Under Dose	1	10%
Correct Dose	5	50%
Total Given Dose	10	100%

#### POLYPEPTIDE ANTIBIOTICS

#### COLISTIN

#### DOSING ACCURACY WISE DISTRIBUTION

**Table No. 19:** shows that total no of patients (COLISTIN) according to their dosing accuracy was 12 (100%). Out of which 10 (83%) patients were used correct dose & the rest of which 2 (17%) patients were used over dose.

DOSING ACCURACY	NO. OF PATIENTS	PERCENTAGE
Overdose	2	17%
Underdose	0	0%
Correct Dose	10	83%
Total Given Dose(Pts.)	12	100%

#### **AZOLE DERIVATIVES**

#### FLUCONAZOL



#### DOSING ACCURACY WISE DIATRIBUTION

**Table No. 20:** shows that total no of patient (FLUCONAZOLE) according to their dosing accuracy was 28 (100%). Out of which 15 (54%) patients were used under dose & rest of which 13 (46%) patients were used correct dose.

DOSING ACCURACY	NO. OF PATIENTS	PERCENTAGE
Over Dose	0	0%
Under Dose	15	54%
Correct Dose	13	46%
Total Given Dose	28	100%

**Table No. 21:** DOSING ACCURACY OF THOSE ANTIBIOTICS WHICH WERE USEDIN HOSPITAL BASED ON RENAL CLEARENCE

DRUG NAME	TOTAL NO. OF DOSING (%)	CORRECT DOSE (%)	OVER DOSE (%)	UNDER DOSE (%)
CIPROFLOXACIN	100%	86%	14%	0%
MOXIFLOXACIN	100%	100%	0%	0%
LEVOFLOXACIN	100%	60%	40%	0%
MEROPENEM	100%	75%	23%	2%
DORIPENEM	100%	50%	50%	0%
PIPERACILLIN & TAZOBACTUM	100%	81%	9%	10%
CO-AMOXICLAV	100%	100%	0%	0%
CEFUROXIME	100%	100%	0%	0%
AMIKACIN	100%	86%	0%	14%
AZITHROMYCIN	100%	100%	0%	0%
FOSFOMYCIN	100%	18%	9%	73%
VANCOMYCIN	100%	50%	40%	10%
COLISTIN	100%	83%	17%	0%
FLUCONAZOLE	100%	46%	0%	54%

#### DISCUSSION

In the study 305 patients were included where 145 patients were male & 160 patients were female. The study was performed in a 200 bedded tertiary care teaching hospital in Kolkata and it carried out for 5 months. Patients who were admitted in ICU and wards were included in this study. These 305 patients data were reviewed throughout the study and analyze as gender wise, age-group wise and dosing accuracy-wise. These all analyze show that...

In this study it shows that total no of patients included in the study were 305 (gender-wise distribution). Out of which 160 were female patients & the remaining 145 were male patients. This gender wise analysis shows that 52.45% patients were female & 47.55% patients were male.

Our study was similar to Lipsky BA *et al*; according to their study 55.79% participants were female & 44.21% of participants were male.<sup>5</sup>

We found that total no patients included in the study were 305 (age group wise distribution). Out of which more than 50 age group patients were 259 & 21-50 age group patients were 43 and the rest of the patients were less than 20 age group patients 3. The age group wise analyze shows that 85% patients were more than 50 aged, 14.10% patients were 21-50 aged and 0.90% patients were less than 20 aged. This study were similar to Lipsky BA *et al*; according to their study 79% patients were more than 50 aged, 18 % patients were 21-50 aged, 3% patients were less than 20 aged.<sup>5</sup>

Study shows that total no of patients (ciprofloxacin) according to their dosing accuracy about the study was 7. Out of which 6 (86%) patients were used correct dose & rest of which 1 (14%) patients were used over dose. So 14% patients needed dosing adjustment.

This study were similar to Lee JH *et al*; according to their study 85% patients were used correct dose.<sup>6</sup>

This study shows that total no of patients (levofloxacin) according to their dosing accuracy about the study was 10. Out of which 6 (60%) patients were used correct dose & rest of which 4 (40%) patients were used over dose. Here 40% patients needed dosing adjustment.

Our study were similar to Thomson AH *et al*; according to their study 33.7% patients needed dosing adjustment.<sup>7</sup>

This study also shows that total no of different type of  $\beta$ -lactum antibiotics used in total patients were 208 (100%). Out of which 104 (50%) patients were used meropenem & 2 (1%) patients were used doripenem, 57 (27%) patients were used piperacillin & tazobactum 29 (14%) patients were used cefuroxim and rest of 16 (8%) patients were used co-amoxiclav.

This study were similar to Lee JH *et al*; according to their study 49% patients were used meropenem & 2% patients were used doripenem, 28% patients were used piperacillin & tazobactum 15% patients were used cefuroxim and rest of 6% patients were used co-amoxiclav.<sup>6</sup>

In this study statistics shows that total no of patients (co-amoxiclav) according to their dosing accuracy about the study was 16 (100%) used in correct dose.

Citation: Prolay Paul et al. Ijppr.Human, 2021; Vol. 20 (3): 211-229.

Our study were similar to Willemijn L. Eppenga *et al*; according to their study 51% patients were used meropenem & 5% of patients were used doripenem, 22% patients were used piperacillin & tazobactum.<sup>8</sup>

Total no of given (amikacin) dosage according to the patients about the study (dosing accuracy wise distribution) were 7 out of which were correct dosage 6(86%) & rest of which was under dosage 1(14%).

Our study were similar to Ohtani H *et al;* according to their study Total no of given (amikacin) dosage according to the patients about the study (dosing accuracy wise distribution) were 10 out of which were correct dosage 7 (70%) & rest of which was under dosage 3 (30%).<sup>9</sup>

Study shows that total no of given doses to patients (vancomycin) according to their dosing accuracy about the study was 10 (100%). Out of which 5 (50%) patients were used correct dose & 4 (40%) patients were used over dose & rest of the patients were used underdose.

Our study was similar to Mingeot-Leclercq MP *et al*; according to their study that total no of given doses to patients (vancomycin) according to their dosing accuracy about the study was 10 (100%). Out of which 7 (70%) patients were used correct dose & 3 (30%) patients were used over dose & rest of the patients were used underdose.<sup>10</sup>

#### **CONCLUSION:**

It was a prospective observational study on the dosing accuracy of antibiotics based on Creatinine Clearance in a 200 bedded tertiary care teaching hospital in Kolkata from March to July. The study was carried out in different wards & ICUs. This study especially assesses the dosing accuracy of different antibiotics and its suspected outcome among the patients admitted in hospitals. In this study, we collected 305 patients data. These 305 patients data were reviewed throughout the study period. The study provides us a detail information about antibiotic dosing accuracy based on patients renal clearance. Renal clearance of the patients was calculated with the help of Cockcroft-Gault Formula and different standard antibiotics dosing guidelines were followed to determine the accuracy. According to this study the dosing accuracy of different antibiotics are comparatively better in ICUs than wards, among carbapenems and beta-lactum are commonly used in hospital. In carbapenems, meropenem is mostly use in hospital. The meropenem's dosing accuracy was 75% correct and 25% incorrect in which 23% over dose and 2% underdose. In beta-lactum, piperacillin &

tazobactum is also mostly use in hospital and its dosing accuracy was 81% correct and 19% incorrect, which was the sum of 9% over dose and 10% underdose. In quinolones, ciprofloxacin and levofloxacin are mostly use in hospitals and their dosing accuracy were 14% overdose, 86% correct dose and 40% over dose, 60% correct dose. These drugs needed the dosing adjustment. So, a standard antibiotic dosing guideline should be introduced in the hospital to avoid overdosing and underdosing. While over dosing of antibiotics may cause serious ADR and underdosing of antibiotics may leads to antibiotic resistance in the future.

#### Abbreviation:

CrCl = creatinine clearance

GFR = Glomerular Filtration Rate

ICU = Intensive Care Unit

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