

## Original Research

# High prescription of antimicrobials in a rural district hospital in India

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### ABSTRACT\*

**Background:** The World Health Organization (WHO) recommends surveillance of antibiotic use as part of the strategy to fight against antimicrobial resistance. However, there is little information about the antibiotic consumption in developing countries, especially in rural areas.

**Objective:** The objective of this study was to describe the antimicrobial consumption in a rural hospital in India

**Methods:** The study was performed in a district hospital situated in Anantapur, Andhra Pradesh. In accordance with WHO recommendations, we used the defined daily dose (DDD) methodology to measure the antibiotic use during one year (from 1st August 2011 to 1st August 2012). The antibiotic use was measured using DDDs/100 admissions and DDDs/100 patient-days for inpatients, and DDDs/100 visits for outpatients.

**Results:** During the study period, there were 15,735 admissions and 250,611 outpatient visits. Antibiotics were prescribed for 86% of inpatients and 12.5% of outpatients. Outpatient prescriptions accounted for 2/3 of the overall antibiotic consumption. For inpatients, the total antibiotic use was 222 DDDs/ 100 patient-days, 693 DDDs/ 100 admissions and the mean number of antibiotics prescribed was 1.8. For outpatients, the total antibiotic use was 86 DDDs/ 100 outpatient visits and the mean number of antibiotics prescribed was 1.2. The most common antibiotics prescribed were aminopenicillins and 3rd generation cephalosporins for inpatients, and tetracyclines and quinolones for outpatients. In a sample of patients with diarrhoea or upper respiratory tract infections (URTI), the proportion of patients who received antibiotics was 84% (95% confidence interval [CI], 67-93) and 52% (95% CI, 43-62), respectively.

**Conclusion:** In this rural setting, the use of antimicrobials was extremely high, even in conditions with a predominantly viral aetiology such as diarrhoea or URTI.

**Keywords:** Anti-Bacterial Agents; Drug Resistance, Bacterial; Drug Utilization; Inappropriate Prescribing; Rural Health; India

### INTRODUCTION

While antimicrobial resistance is a major concern worldwide, it is especially important for developing countries because of the high mortality associated with common bacterial infections in resource-limited settings.<sup>1</sup> Antibiotic pressure is the single most important factor for the selection of resistant bacteria and the appearance of new mechanisms of resistance<sup>2</sup>, but studies describing antibiotic consumption in developing countries are scarce.

In India, antibiotic spending has increased by about 40% between 2005 and 2009.<sup>2</sup> Although more than two thirds of the Indian population are rural residents, little is known about the consumption patterns of antibiotics in rural India because previous studies have been performed in urban areas or tertiary hospitals.<sup>2-5</sup> The aim of this study was to describe the consumption of antibiotics in a district hospital situated in a rural area of India. In addition, we also investigated the proportion of patients who received antibiotics in a sample of cases diagnosed with diarrhoea or upper respiratory tract infection (URTI), because these conditions are predominantly of viral aetiology.<sup>6</sup>

### METHODS

#### Setting

The study was performed at the Rural Development Trust General Hospital, a non-profit 220-bed hospital in Bathalapalli, Andhra Pradesh, India. Bathalapalli is a village of 9810 habitants located in the district of Anantapur. In Anantapur, 72% of the population lives in rural areas and 36% are illiterate.<sup>7</sup>

The hospital has an average occupancy rate of 90% and a small 7-bed Intensive Care Unit. The hospital belongs to a non-governmental organization called Fundación Vicente Ferrer – Rural Development Trust, which provides free consultation and medicines at reduced prices to people of low socio-economic status. The hospital has a Microbiology Department, which provides antimicrobial susceptibilities of bacterial infections, but there is not a stewardship programme to control the use of antibiotics.

#### Study design

We collected data on antibiotic prescriptions from the Hospital Database during one year (from 1<sup>st</sup> August 2011 to 1<sup>st</sup> August 2012) for avoiding seasonal variation of antibiotic use.

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Table 1: Description of the total antibiotic consumption and by hospital departments.

		Total	Medicine	O&G	Surgery
<b>Inpatients</b>					
	Admissions (N)	15735	2901	9575	3259
	Any antibiotic (%)	86	62.9	92.2	88.4
	N of antibiotics (mean)	1.81	2.2	1.67	1.99
	Days of admission (mean)	3.1	4.3	2.5	3.9
	DDDs/100 patient-days	221.9	153.2	294.8	150.8
	DDDs/100 admissions	692.5	652.3	739.7	589.5
<b>Outpatients</b>					
	Visits (N)	250611	120241	88264	42106
	Any antibiotic (%)	12.5	14.91	8.98	13.04
	N of antibiotics (mean)	1.21	1.18	1.24	1.26
	DDDs/100 visits	86.16	104.68	58.47	91.31

DDDs; defined daily doses; N, number; O&G, Obstetrics and Gynaecology.

Following recommendations from the World Health Organization (WHO), the measurement of antibiotic consumption was performed using the Anatomic Therapeutic Classification (ATC) index with the defined daily dose (DDD) methodology.<sup>8</sup> The ATC/DDD methodology is a tool for drug utilization research in order to improve quality of drug use by allowing comparison of drug consumption statistics at international or other levels. ATC is a code to classify drugs according to their therapeutic and pharmacological use. The DDD is the assumed average maintenance dose per day for a drug used for its main indication in adults.<sup>8</sup> The DDD provides a fixed unit of measurement independent of price and dosage form (e.g. tablet strength) enabling researchers to assess trends in drug consumption and to perform comparisons between population.<sup>8</sup> As the DDD methodology is not adequate for studying drug use in children, paediatric patients were excluded from the study.

For inpatients, we used two parameters to measure the antibiotic consumption, the DDDs/100 admissions and the DDDs/100 patient-days, being patient-days the total number of days of admission. For outpatient, we used the DDDs/100 visits to the outpatient clinics.

For studying the inappropriate use of antibiotics in a sample of outpatients, we studied the prescriptions of patients who were diagnosed with diarrhoea or URTI from March 1<sup>st</sup> 2012 to March 14<sup>th</sup> 2012.

The study was approved by the Hospital Ethical Committee. Statistical analysis was performed using Stata Statistical Software (Stata Corporation. Release 11. College Station, Texas, USA).

## RESULTS

During the period of the study, the total number of antibiotic DDDs prescribed was 324,882; 108,962 (33.5%) DDDs in inpatients and 215,920 (66.5%) DDDs in outpatients. Description of antibiotic consumption by DDDs/ 100 patient-days, DDDs/ 100 admissions, DDDs/ 100 outpatient visits, and the proportion (percentage) of patients who received any antibiotic is presented in Table 1.

Overall, 86% of inpatients received antibiotics. Surgical specialities had higher proportion of inpatients on antibiotics than Medicine. However, for those patients who received antibiotics, the number of antibiotics prescribed was higher in the Medicine Department. The number of DDDs/100 patient-days in inpatients was 222. The highest number of DDDs/100 patient-days was observed in the Department of Obstetrics and Gynaecology (O&G).

Overall, 12.5% of outpatients received antibiotics and the number of DDDs/100 outpatient visits was 86. The highest prescription of antibiotics was observed in the Medicine Department, followed by Surgery and O&G.

Through patient exit interviews, we identified 31 patients diagnosed with diarrhoea and 107 patients diagnosed with URTI. The proportion of patients who received antibiotics was 83.9% (Wilson 95% confidence interval, 67.3-92.9) for diarrhoea and 52.3% (Wilson 95% confidence interval, 43-61.6) for URTI.

Table 2 describes the consumption of antibiotics that accounted for the 90% of the prescriptions (drug utilization 90%) overall and by hospital departments.

Table 2: Description of the most utilized antibiotics (drug utilization 90%) in inpatients and outpatients.

antibiotic group	DDDs/100 patient-days (IP)				DDDs/100 admissions (IP)				DDDs/100 outpatient visits			
	Total	Med	O&G	Surg	Total	Med	O&G	Surg	Total	Med	O&G	Surg
Aminopenicillins	171.73	11.07	313.43	60.32	536.02	47.13	786.33	235.79	18.03	18.05	8.6	37.75
Aminopenicillin & enzyme inhibitor	19.95	39.6	3.55	31.82	62.27	168.62	8.91	124.36	20.23	25.27	5.17	37.41
3 <sup>rd</sup> generation cephalosporins	76.94	47.15	117.54	29.28	240.16	200.78	294.89	114.44	17.43	20.45	15.23	13.4
Lincosamides	1.41	2.17	0.23	2.91	4.41	9.23	0.57	11.38	0.05	0.03	0.03	0.13
Tetracyclines	17.06	59.75	2.84	2.48	53.26	254.46	7.12	9.7	47.28	67.1	29.14	28.7
Imidazoles	23.61	22.74	13.94	42.67	73.68	96.86	34.98	166.78	16.84	15.14	15.79	23.87
Macrolides	4.99	7.54	5.43	1.7	15.59	32.13	13.62	6.66	7.36	9	7.06	3.32
Quinolones	11.57	30.42	1.66	12	36.13	129.54	4.15	46.91	25.24	31.26	19.57	19.92
Co-trimoxazole	2.04	2.71	0.56	4.18	6.36	11.53	1.4	16.33	1.01	1.06	0.55	1.84
Aminoglycosides	9.44	9.55	4.09	19.41	29.46	40.67	10.26	75.89	0.3	0.31	0.09	0.69

DDDs, defined daily doses; IP, inpatients; Med, Medicine; O&G, Obstetrics and Gynaecology; Surg, Surgery.

In patients admitted to O&G or Surgery, the most commonly prescribed antibiotics were aminopenicillins, followed by 3<sup>rd</sup> generation cephalosporins and imidazoles. In patients admitted in Medicine, the most commonly prescribed antibiotics were tetracyclines, 3<sup>rd</sup> generation cephalosporins, aminopenicillin with enzyme inhibitor (amoxicillin/clavulanic acid) and quinolones.

In outpatients, the most commonly prescribed antibiotics were tetracyclines, quinolones, aminopenicillins with enzyme inhibitor, aminopenicillins, 3<sup>rd</sup> generation cephalosporins and imidazoles. Antibiotics effective against anaerobes such as imidazoles and aminopenicillins with enzyme inhibitor were more commonly prescribed in the Surgical Department.

## DISCUSSION

To our knowledge, this is one of the first studies to investigate the prescribing of antibiotics in a rural hospital in India using the methodology recommended by the WHO.

Among inpatients, the number of DDDs/ 100 patient-days was 222, which is four times higher than the ones reported in Europe and China.<sup>9,10</sup> In a study from Ujjain, MP India, the proportion of admitted patients who received any antibiotic was 78-82%, which is similar to the one found in our hospital.<sup>11</sup>

A comparison of our outpatient antibiotic use with western countries is difficult because other studies have utilized DDDs/1000 inhabitants daily to measure outpatient antibiotic consumption.<sup>12,13</sup> The proportion of patients with diarrhoea or URTI who received antibiotics was higher than previously reported in other sites.<sup>14-16</sup> However, the proportion of outpatients who received any antibiotic was similar to the ones described in other urban Indian sites.<sup>2-5</sup> In a study investigating the antimicrobial prescription in outpatients with symptoms of acute infection at four sites in India, the proportion of patients from rural areas who received antibiotics was 71.7% (95% CI, 68.6-74.8).<sup>6</sup>

Previous studies have shown that antibiotic exposure has an important role in the emergence of antimicrobial resistance in the population.<sup>17,18</sup> The high consumption of antibiotics described in the present study could have an important impact on the appearance of antimicrobial resistance in the community. In fact, we have recently described high rates of methicillin resistant *Staphylococcus aureus* and third-generation cephalosporin resistant Gram negative bacteria in our setting.<sup>19,20</sup>

Western countries have responded to the problem of antimicrobial overuse by implementing institutional programmes to optimize clinical outcomes while reducing the risks associated with antibiotic overuse, including toxicity and the emergence of resistance.<sup>9,21</sup> The combination of antimicrobial stewardship and infection control programmes have demonstrated to limit the emergence and transmission of resistant bacteria

and to reduce the direct and indirect health-care costs associated with the misuse of antimicrobials.<sup>21</sup> Ideally, these programmes should include a clinical microbiologist, an infectious disease physician, a clinical pharmacist and an infection control professional. The strategies to improve the use of antimicrobial are multiple: direct interaction and feedback to the prescribers; formulary restriction and pre-authorization of certain antimicrobials; educational activities; clinical protocols for empirical treatment of infections taking into account local resistances; de-escalation of empirical therapy; dose optimization of antimicrobials; and parental to oral conversion.<sup>21</sup>

The study has some limitations. The use of DDDs has been criticized because it has shown poor correlation with prescribed daily doses in some settings. However, prescribed daily doses may vary among health care facilities and DDDs allow comparison among hospitals or clinics even when prescribed daily doses are different. In addition, this is a single site study of antibiotic consumption in rural India, so our results must be confirmed by studies from other rural sites.

## CONCLUSIONS

The study shows that, in our rural setting, the consumption of antimicrobials in outpatients and inpatients is higher than the ones reported in other countries, but similar to the ones reported in tertiary hospitals and urban areas of India. If these results are confirmed in other sites, the results of this study indicate that there is an urgent need to improve the prescription of antibiotics in rural India.

## CONFLICT OF INTEREST

The authors declare no conflict of interest.

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## ELEVADA PRESCRIPCIÓN DE ANTIMICROBIANOS EN UN HOSPITAL RURAL COMARCAL EN INDIA

### RESUMEN

**Antecedentes:** La Organización Mundial de la Salud (OMS) recomienda la vigilancia del uso de antibióticos como parte de la estrategia de lucha contra la resistencia a antibióticos. Sin embargo, existe poca información del consumo de antibióticos en países en vías de desarrollo, especialmente en áreas rurales.

**Objetivos:** El objetivo de este estudio fue describir el consumo de antimicrobianos en un hospital rural de India.

**Métodos:** El estudio se realizó en un hospital comarcal situado en Anantapur, Andhra Pradesh. De acuerdo con las recomendaciones de la OMS, usamos la metodología de la dosis diaria definida (DDD) para medir el uso de antibióticos durante un año (del 1 de agosto de 2011 a 1 de agosto de 2012). El uso de antibióticos se midió usando las DDD/100 ingresos y las DDD/100 pacientes-día para internados y DDD/100 visitas para los externos.

**Resultados:** Durante el período de estudio, hubo 15.735 ingresos y 250.611 consultas externas. Se prescribieron antibióticos en el 86% de los internados y en el 12,5% de los externos. Las prescripciones de los externos sumaron

2/3 del consumo total de antibióticos. Para internados, el uso total de antibióticos fue de 222 DDD/100 pacientes-día, de 693 DDD/100 ingresos y el número medio de antibióticos prescritos fue de 1,8. Para los pacientes externos, el uso de antibióticos fue de 86 DDD/100 visitas y la media de antibióticos prescritos fue de 1,2. Los antibióticos más frecuentemente prescritos fueron las aminopenicilinas y las cefalosporinas de 3ª generación para los internados, y las tetraciclinas y quinolonas para los externos. En una muestra de pacientes con diarrea o infecciones del tracto respiratorio superior (URTI), la proporción de pacientes que recibió antibióticos fue del

84% (intervalo de confianza [IC] 95% 67-93) y del 52% (IC95% 43-62), respectivamente.

**Conclusión:** En un entorno rural, el consumo de antibióticos fue extremadamente elevado, incluso en situaciones de una etiología predominantemente vírica como diarrea o URTI.

**Palabras clave:** Antibacterianos; Farmacorresistencia Bacteriana; Utilización de Medicamentos; Prescripción Inadecuada; Salud Rural; India

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