

# Occurrence of Microbial Resistance in Blood Cultures in a Teaching Hospital before and after the Restrictive Measure for the Commercialization of Antimicrobials in Brazil

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## Research Article

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## Abstract

Bacterial resistance to antimicrobial drugs (ATM) has become a global public health problem. The collegiate board of the National Health Surveillance Agency (ANVISA) through RDC 44, published on October 26, 2010, determined that prescribed antibiotics can only be dispensed with special control prescription, aiming to restrict the free access to these drugs and minimize the microbial resistance. The present study aims to identify microbial resistance in blood culture in hospitalized patients before and after the implementation of restrictive measurement. We observed decrease in the occurrence of blood culture microbial resistance in Phase II (0,62 for 100 people day) compared with Phase I (0,75 for 100 people day).

**Keywords:** Anti-Bacterial agents; Prescription drug overuse; Legislation & jurisprudence; Drug resistance; Pharmacovigilance

**Abbreviations:** ATM: Antimicrobial Drugs; ANVISA: National Health Surveillance Agency; HRTN: Hospital Risoleta Tolentino Neves; WHO: World Health Organization.

## Introduction

Bacterial resistance to antimicrobials drugs (ATM) is serious threat to global public health, widely described in the literature [1,2]. Besides that, an expressive increase in

the consumption of ATM is identified in the 2000 decade in emerging countries [3].

Among the strategies to minimize the development of resistance, the reduction of the prescription of ATM and the implementation of strategies that stimulate rational use have deserved prominence [4,5]. The optimization of the use of ATM is among the five objectives of the Global Action Plan of the World Health Organization (WHO) to control microbial resistance [6].

In Brazil, up to 2010, ATM could be acquired by the community only with the presentation of a prescription, which favor self-medication and compromise a rigorous control. The collegiate board of the National Health Surveillance Agency (ANVISA) through RDC 44, published on October 26, 2010, determined that prescribed antibiotics can only be dispensed with special control prescription, aiming to restrict the free access to these drugs and minimize the microbial resistance [7].

Studies indicate that ATM use in hospitals affects the community microbial resistance and vice versa [8,9]. Therefore it is relevant to evaluate the impact of the implementation of restrictive measures for the marketing of these medicines in both environments. Given the context that hospital infections raise health expenditures and cause harm to patients, our study aimed to compare the occurrence of microbial resistance in blood culture in a hospital environment before and after the implementation of the restrictive measure of ANVISA for the commercialization of ATM in Brazil.

## Methods

### Study Design, Location and Population

This is a quasi-experimental study including adult patients admitted in a Brazilian university hospital located in Belo Horizonte, Minas Gerais from May 2010 to July 2011. The Hospital Risoleta Tolentino Neves (HRTN) is a general public emergency hospital, reference for the northern region of Belo Horizonte and neighboring municipalities that has about 330 beds. Approximately 10.000 patients are attended each month, which about 13.0% are hospitalized in the same institution.

We included patients over 18 years of age, for whom blood culture exams were requested due to suspected hospital infection or routine procedures to identify bacterial colonization. Patients with diagnosis of bacterial infection at admission or up to 72 hours after hospitalization, women hospitalized for childbirth and puerperium, and patients transferred from another hospital or with length of stay of less than 72 hours were excluded.

This study consisted of two phases: The first (Phase I) included patients admitted to the HTRN from May to October 2010, period before the restrictive measure for the commercialization of ATM, and the second (Phase II) was formed by patients admitted between February and

July 2011, after the implementation of the measure of ANVISA. The option for this period aimed to obtain symmetrical time intervals that minimized the interference of non-controllable factors such as turnover of professionals, shortage of the supply of medications and influence of non-standardization of procedures to conduct the examinations of the institution. The team responsible for controlling infections associated with health care at the institution and the clinical body did not undergo alterations during the study period, but a change was recorded in the laboratory that performed the exams in the HRTN in the second semester of 2011 (period after data collection). No shortage of supply of medications occurred during the study periods.

### Definition of Study Variables

The outcome of interest was blood infection by a microorganism resistant to ATM, evidenced by positive results of *in vitro* blood culture of microorganisms and result of the sensitivity test to Antimicrobial agents (*in vitro* antibiogram), and interpreted as "resistant" in patients with hospitalization stay exceeding 72 hours [10]. In this study, microbial resistance was defined as the antibiotic resistance from a clinical point of view, considering a higher probability of therapeutic failure when an infection by a given microorganism is treated with a class of antibiotics customarily used in clinical practice, identified by resistance results in the antibiogram [11].

We also identified the total number of blood culture exams requested by the patient, the resistant microorganisms and the resistance profile. The procedures of culture collection in the HRTN occurred in case of clinical suspicion of infection or through the culture of axillary and anophanous swab, whose institutional protocol recommended weekly collection for patients with hospitalization time exceeding 15 days, even without signs or symptoms of infection.

### Data Collection and Analysis

The information on bacterial resistance and others variables was collected from secondary data, through the review of the patient's electronic record and the generation of computerized reports.

Regarding the identification of microbial resistance, a computerized report of all the culture exams performed for the patients under study was generated, then the results were checked. In specific cases, the information

was complemented with records of the hospital infection control committee on the resistance profile in the institution.

The unit of microorganism resistant was 100 people day, identified for: number of microorganism resistance /hospital charge time (days) x 100. This project was approved by the Human Research Ethics Committee of the Federal University of Viçosa (Opinion 176/2012).

## Results

During the study period, culture exams were requested for 413 patients in Phase I and for 410 patients in Phase II. The average age was 61, 0 years (SD: 18,6) in Phase I and 62, 1 years (SD: 18,4) in Phase II, with most prevalent male (53,9%). The average period of hospitalization was 29, 4 days (SD: 22,8) and 30,0 days (SD: 23,9) in the Phases I and II, respectively.

Of the total tests performed (Phase I: 2046; Phase II: 1928), 324 and 408 isolates were identified in Phases I and II, respectively. 105 (32.40%) isolates in Phase I showed resistance, while in Phase II, resistance was identified in 88 (21.56%) isolates. We observed decrease in the occurrence of blood culture microbial resistance in Phase II (0, 62 for 100 people day) compared with Phase I (0, 75 for 100 people day).

## Discussion

Few Brazilian studies have been conducted in order to identify the contributions of the restrictive measure in the control of infections, and most of them are directed to the analysis of the sales of ATM in drugstores [12,13].

The criterion used to define infection as of hospital nature was its registration in a period equal to or greater than 72 hours of hospital stay, in order to exclude cases of community infection. This criterion is defined in Brazil by Ordinance 2,616 of May 12, 1998 [11] and has been adopted in different studies [14,15]. It is not possible to guarantee that some cases detected have not been originated in the community.

Another study conducted by the same group of researchers suggests that the implementation of the restrictive measure of the commercialization of antimicrobials by ANVISA reduced the incidence of hospital infection by a resistant microorganism [16].

Despite findings, we believe to be important identify the impact of the restrictive measure on specific infections such as blood culture. Although we identified a decreased in microbial resistance in blood culture, broader statistical analyzes are required. These are partial results of a larger study has being conducted in Brazil.

## Conclusion

We observed decrease in the occurrence of microbial resistance in blood culture before and after the implementation of the restrictive measure of ANVISA for the commercialization of ATM in Brazil. However, broader statistical analyzes are required.

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