BACTERIOLOGICAL PROFILE AND DRUG RESISTANCE PATTERNS OF BLOOD CULTURE ISOLATES AT A SECONDARY CARE HOSPITAL IN BRAZIL

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To The Brazilian Journal of Infectious Diseases

Subject: SUBMISSION OF NEW MANUSCRIPT FOR EVALUATION

Dear Editor,

I am enclosing herewith a manuscript entitled "**BACTERIOLOGICAL PROFILE AND DRUG RESISTANCE PATTERNS OF BLOOD CULTURE ISOLATES AT A SECONDARY CARE HOSPITAL IN BRAZIL"** for publication in Brazilian Journal of Infectious Diseases as an Original Article.

This project was approved by the Ethics Comitee of Instituto de Medicina Integral Prof. Fernando Figueira (CEP-IMIP nº 3659-13) and received a financial support from PIBIC-CNPq / IMIP. With the submission of this manuscript I would like to undertake that the above mentioned manuscript has not been published elsewhere, accepted for publication elsewhere or under editorial review for publication elsewhere; and that my Institute's representative is fully aware of this submission. I also confirm that the manuscript content represents the views of the coauthors.

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ABSTRACT

Objective: The purpose of this study is to analyze the most prevalent microorganisms causing bacteremia and their resistance profiles in a secondary care hospital in Pernambuco, Brazil.

Methods: This was a transversal, descriptive study, based on positive blood cultures collected from patients admitted in the hospital from January to December of 2012.

Results: About 1056 bacteria were isolated from 915 blood cultures (86% monomicrobial and 14% polymicrobial). The most prevalent microorganisms were coagulase-negative Staphylococci (53.2%), *Staphylococcus aureus* (10.2%), *Acinetobacter baumannii* (7.9%), *Klebsiella pneumoniae* (5.1%) and *Enterococcus faecalis* (3.5%). Coagulase-negative Staphylococci were oxacillin-resistant in 83.1% and *S. aureus* was in 61.1% of cases, but both were 100% susceptible to vancomycin and linezolid. There was no vancomycin resistant *Enterococcus spp*. Enterobacteriaceae were multidrug resistant in 30.2% of cases, and there was extended-spectrum beta-lactamases and carbapenemase production in 12.6% and 13.6%, respectively. *K. pneumoniae* was multidrug resistant in 59.3%, and produced extended-spectrum beta-lactamases in 42.6% and carbapenemase in 16.7%. Almost 87% of *Acinetobacter baumannii* isolates were multidrug resistant, and imipenem resistance rate was 81.2%. Except for *Serratia marcescens*, no other gram negative was resistant do polymyxin B.

Discussion: High frequencies of drug resistance were found among the most frequent microorganisms. These strains are susceptible only to a few broad spectrum antibiotics, which leaves limited options for treatment in critically ill patients.

Keywords: Bacteremia, drug resistance, anti-bacterial agents.

Introduction

Nosocomial infections are an important cause of morbidity and mortality throughout the world, increasing length of hospital stay and costs (1-3). Bloodstream infections (BSI) correspond to 9.9-14.2% of nosocomial infections (4, 5), and it is often necessary to initiate an empirical antibiotic treatment in critically ill patients before the cultures results are available. However antimicrobial therapy can exert selective pressure, and the indiscriminate use of antibiotics may lead to multidrug resistance(6).There have been reports of multidrug resistant strains of the most common nosocomial pathogens, such as *Staphylococcus aureus* (*S. aureus*), *Enterococcus spp*., *Escherichia coli* (*E. coli*), *Klebsiella pneumoniae* (*K. pneumoniae*), *Acinetobacter baumannii*(*A. baumanii*) and *Pseudomonas aeruginosa* (*P. aeruginosa*) (7-9).

The prevalence of pathogens and their resistance patterns may vary in different hospitals (10). Therefore knowing the most frequent pathogens becomes necessary for effective antibiotic treatment, decreasing length of hospital stay, morbidity and mortality of patients (11). Thus, the purpose of this study is to analyze the most prevalent microorganisms causing bacteremia and their resistance profiles in a secondary care hospital in Pernambuco, Brazil.

Materials and methods

Design and setting

This was a transversal, descriptive study, based on positive blood cultures collected from patients admitted in a public secondary hospital in Pernambuco, Brazil, from January to December of 2012.The hospital has 180 beds, distributed in five sectors: Intensive care unit (29), emergency (34), clinical ward (30), general surgery ward (29) and orthopedic ward (58).

Sample collection and processing

The blood samples were cultured by automated methods, using Bactec FX, and the microbiological identification and antimicrobial susceptibility were performed using Vitek 2 automated system. Each pathogen was classified as susceptible, intermediate or resistant to each antibiotic tested. Enterobacteriaceae were also tested for extended-spectrum beta-lactamases (ESBL) and classified as probable carbapenemase producers or not.

Analysis

It was included in the study all positive blood cultures in the hospital in the year of 2012, except those positive for fungus or mycobacteria. There were 915 positive samples and 1056 isolates. Multidrug resistance was defined as non-susceptibility to at least one agent in three or more antimicrobial categories, and oxacillin-resistant *S. aureus* isolates were categorized as multidrug resistant (MDR) as well (12). The isolates were also categorized by the hospital sector: ICU, wards and emergency.

Results

About 1056 bacteria were isolated from 915 blood cultures, from which 86% were monomicrobial and in 14% were polymicrobial. The most prevalent microorganism was coagulase-negative staphylococcus (CoNS), performing 53.2% of the total, followed by *S. aureus* (10.2%), *A. baumannii* (7.9%) and *K. pneumoniae* (5.1%). The prevalence of the most common microorganisms is shown in Figure 1.

The rates of resistance to carbapenems and cephalosporins were considerable among gram negative bacilli (GNB) (Table 1). Both *A. baumannii* and *S. marcescens* were

resistant to carbapenems and cephalosporins in more than 80% of cases, but they were mostly susceptible to gentamicin. *P. aeruginosa* was resistant to cephthazidimin 45.5% of cases, but only 13.6% of the isolates tested for piperacillin-tazobactam were resistant. Except for *S. marcescens*, no other GNB was resistant do polymyxin B. Gram positive cocci (GPC) were all susceptible to vancomycin and linezolid. There was a high frequency of oxacillin-resistant CoNS(83.1%) and *S. aureus* (61.1%) (Table 2)

The frequency of MDR GPC is shown in Figure 2, and the percentages of multidrug resistance, ESBL and carbapenemase producers among GNB are shown in Figure 3. High rates of multidrug resistance are shown among the most common bacteria, especially *A. baumannii*, *S. marcescens*, CoNS and *S. aureus*.

The ICU was responsible for 49.3% of isolates, emergency for 38.4% and wards for 12.2%. The most prevalent isolate is CoNS in all three sectors, but the frequency of the other pathogens varied between them. *A. baumannii* was more prevalent in ICU and wards comparing to emergency, while *S. aureus* was less prevalent in ICU. Gram negative bacteria were less frequent in emergency comparing to wards and ICU (Table 3).

Discussion

Although there have been an increase in gram negative bacteria reported in several studies (5, 13, 14), there is still a prevalence of gram positive organisms in some of them.(4, 15-17)Our study shows similar results, in which 70.8% of bacteria are gram positive versus 29.2% of gram negative. The most prevalent isolates were CoNS (53.2%), S. aureus (10.2%), A. baumannii (7.9%) and K. pneumoniae (5.1%). Although P. aeruginosa is an important pathogen reported in many studies, it represented only 2.1% of all isolates in our study.

A multicenter study performed in the US and another one in Europe also found CoNS as the most common bacteria, as well as studies in Colombia and India, but in lower frequencies (16.7-39.6%)(4, 5, 14, 17, 18). Other studies showed S. aureus as the most common bacteria, including a multicenter study performed in Brazil(13, 15). High levels of oxacillin resistant CoNS were found in our study (83.1%), but this founding is in consonance with results found in Brazil (13, 19) and other parts of the world (14, 20).

The high prevalence of CoNS could be explained by the fact that these bacteria are often skin colonizers, and the use of external devices predispose to infection caused by them.(21) This group is also the most common cause of contamination of samples, and it is necessary clinical correlation to discriminate whether it is a pathogen or a contaminant(22, 23).

Staphylococcus aureus was resistant to oxacillin in 61.1% of the isolates, similar to other recent studies – varying from 33.4 to 70.6% (13, 15, 16, 18, 24, 25). Because of the high rates of resistance, vancomycin should be considered as a first choice in critically ill patients who need empiric antimicrobial therapy, since there was no isolate resistant do this drug in our study.

Enterococcus spp. was observed in 4.8% of all isolates. There was no vancomycin resistant Enterococcus spp. in this study, in contrast to other studies showing different rates of resistance. A nationwide surveillance study in the US found 60% of vancomycin resistant E. faecium, but only 2% of resistant E. faecalis(18), while other studies show rates up to 29% (26-28).

The prevalence of A. baumannii in this study was 7.9%, and most of them were isolated either in the ICU or in wards, and only 2.9% of them were isolated in emergency. That could be explained by the fact that this species is associated with mechanic ventilation(7), and a significant amount of patients in wards in this hospital comes from the ICU. Almost

87% of the isolates were MDR, and imipenem resistance rate was 81.2%, results in conformity with a global tendency of increasing resistance rates(29-31).

A multicentric surveillance study in America was published in 2004, demonstrating carbapenem resistance rates ranging from 0.7-20% (20). Recent studies have shown that this is no longer a reality: 83% of A baumannii isolates in a study in India were resistant to imipenem(14), similar to our results, 49.5% in Colombia(17), 55.9% in Brazil(13), 54% in Italy(32). This scenario has origin in multiple factors, including the indiscriminate use of carbapenems, and the fact A. baumannii is able todevelop multiple resistance mechanisms(33).

Although the SENTRY study reported Latin America to register the higher rates of ESBL production, reaching 23.9%(20), in this study, there were 12.6% of ESBL producers among Enterobacteriaceae. Similar results were found in a study in Colombia, in which 14.7% were ESBL producers in blood, urine and other samples(34). Other studies in Brazil revealed rates from 22 to 29%(13, 35). Escherichia coli and K. pneumoniae were ESBL producers in 34.6% and 46.2% of the isolates respectively. Similar rates were described in a global surveillance, in which rates around 40% for E. coli and over 50% to K. pneumoniae were published (36).

Carbapenemase production was suspected in 13.6% of all Enterobacteriaceae. Enterobacter spp. and S. marcescens had the highest rates: 46.2% and 87.5%, while carbapenemase production in K. pneumonia was 16.7%. Carbapenem resistance rates seem to be very different in many studies. This founding was high compared 1.1% total carbapenem resistance found in a large study performed in USA(9) and to 1.3% found among K. pneumoniae in a Brazilian study (13), but it was similar to 12.8% among K. pneumonia found in a Colombian study(34) and much lower than 77% found in another

study performed in Colombia(17). That variation might be influenced by the extensive usage of these antibiotics in some hospitals, exerting selective pressure.

Serratia marcescens has proved high resistance rates to most antimicrobials tested, and 91.7% of the isolates were MDR. Gentamicin and Trimethoprim-sulphamethoxazole had the higher susceptibility, while 87.5% were resistant to carbapenems. Those findings differ from the ones described in Latin America: more than 91% of all S. marcescens isolates were susceptible to carbapenems (36).This species is also capable of developing resistance to polymyxin B(37), which explains 95.2% of resistance to that antimicrobial, while all other Enterobacteria tested were susceptible.

A limitation in our study was the fact samples were collected in a secondary hospital, while most of the other studies were performed in tertiary hospitals. Also we analyzed samples collected in one year, and in this period it is not possible to analyze a tendency in drug resistance patterns at this hospital. Finally, we did not correlate these results with characteristics of the patients such as comorbidities and previous hospitalization, which may influence the prevalence of microorganisms found in this study.

Conclusions

These results corroborate the variation in microbiology and resistance patterns among different hospitals, and how important it is to know it to determine the best antimicrobials for empiric treatment in each service. This study provides relevant information to guide empiric therapy in our settings. It also draws attention to the fact there are important MDR strains susceptible only to a few broad spectrum antibiotics, leaving limited options for treatment. This scenario becomes more preoccupying considering the fact only a small number of antibiotics are in development.

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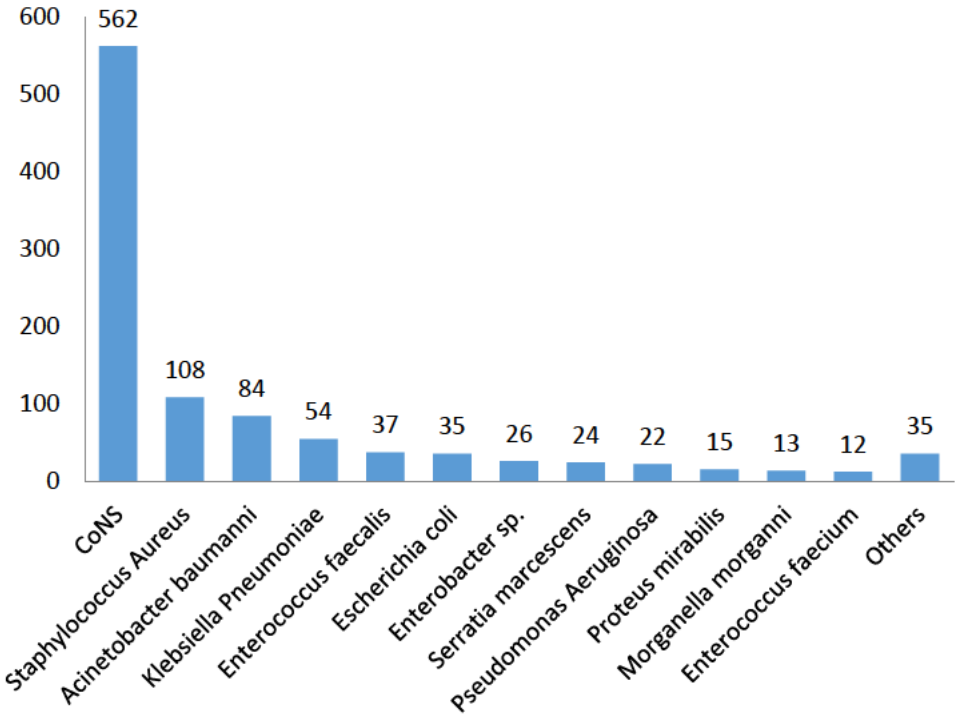

Figure 1. Frequency of microorganisms isolated from blood cultures at a secondary Brazilian hospital in 2012 (n=1056).

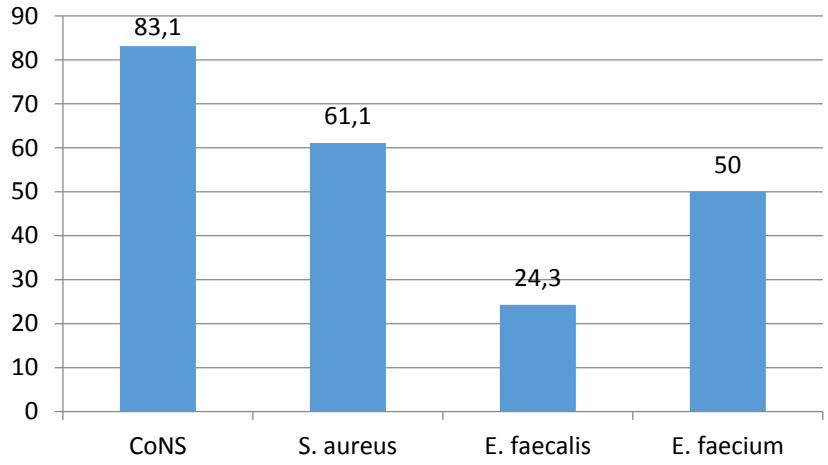

Figure 2. Percentage of multidrug resistance among gram positive cocci isolated from blood cultures at a secondary Brazilian hospital in 2012.

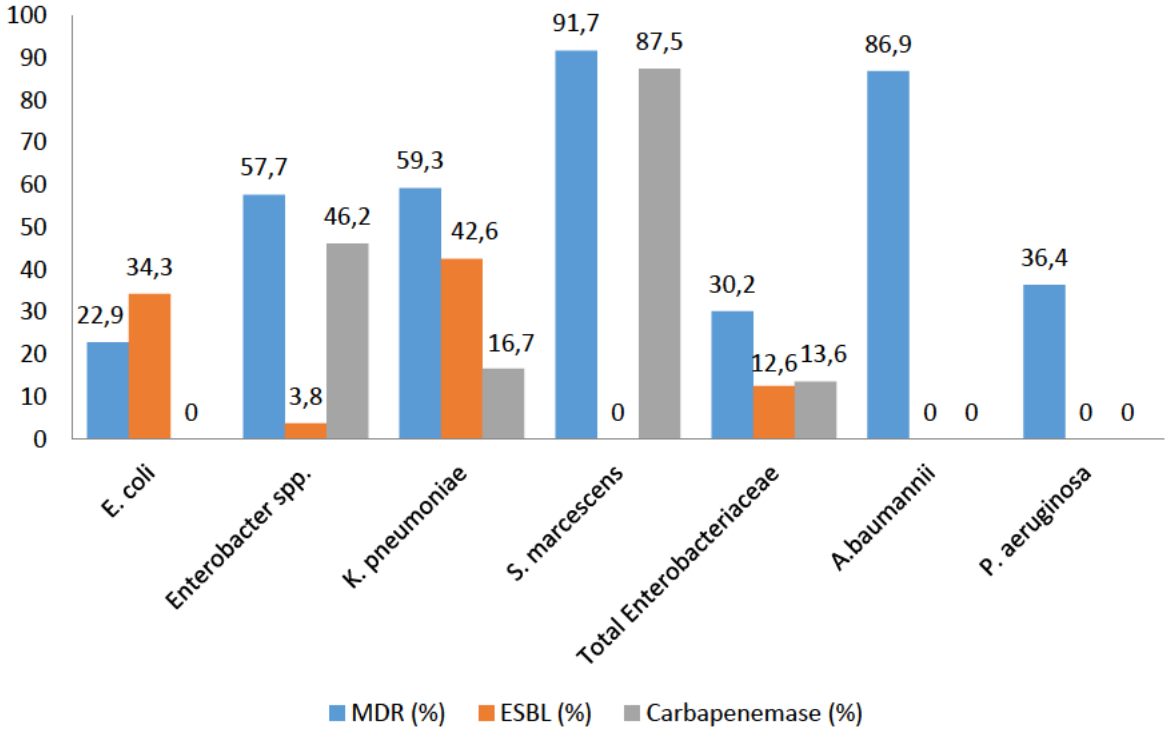

Figure 3. Percentage of multidrug resistance, extended-spectrum beta-lactamases and carbapenemase in gram-negative bacilli isolated from blood cultures at a secondary Brazilian hospital in 2012

Table 1. Resistance of gram negative bacteria to antimicrobial agent

Antimicrobial agent	**Percentage resistance**					
	A. baumannii	P. aeruginosa	K. pneumoniae	E. coli	Enterobacter sp.	S. marcescens
Amikacin	72.6	13.6	5.6	0	19.2	75
Ampicillin-sulbactum	40.5	NT	NT	NT	NT	NT
Cefepime	82.1	40.9	59.3	31.4	42.3	91.7
Ceftazidime	85.7	45.5	59.3	31.4	61.5	83.3
Ceftriaxone	NT	NT	59.3	31.4	60.0	95.8
Ciprofloxacin	84.5	31.8	57.4	37.1	61.5	45.8
Ertapenem	NT	NT	16.7	0	70.6	87.5
Gentamicin	25	36.4	33.3	25.7	30.8	12.5
Imipenem	81.2	31.8	11.1	0	42.3	87.5
Levofloxacin	79.7	NT	57.4	31.4	57.7	37.5
Meropenem	78.6	31.8	13.0	0	42.3	87.5
Piperacillin-tazobactam	81.2	13.6	38.9	2.9	53.9	87.5
Polymyxin B	0	0	0	NT	0	95.2
Trimethoprim-sulphamethoxazole	NT	NT	57.4	44.1	57.7	16.7
Tobramycin	NT	NT	31.5	11.8	36.0	29.2

NT= not tested

Table 2. Resistance of gram positive cocci to antimicrobial agent

Antimicrobial agent	**Percentage resistance**			
	S. aureus	**CoNS**	**E. faecalis**	**E. faecium**
Ampicillin	100	99.2	0	75
Ciprofloxacin	46.3	67.1	45.9	66.7
Streptomycin*	NT	NT	56.8	33.3
Gentamicin	14.8	48.8	29.7*	41.7*
Levofloxacin	44.8	65.7	43.2	66.7
Linezolid	0	0	NT	0
Oxacillin	61.1	83.1	NT	NT
Penicillin	100	99.5	NT	75
Trimethoprim-sulphamethoxazole	7.4	52.7	NT	NT
Tetracycline	20.6	11.8	70.2	16.7
Vancomycin	0	0	0	0

*High level streptomycin, **High level gentamicin, CoNS, coagulase negative staphylococcus, NT, not tested

Table 3. Prevalence of microorganisms by hospital sector

Microorganism	UCI n(%)	Wards n(%)	Emergency n(%)
CoNS	280 (53.7)	53(41.1)	229(56.4)
A. Baumannii	58 (11.1)	14(10.8)	12(2.9)
K. Pneumoniae	34 (6.5)	7(5.4)	11(2.7)
S. Aureus	27 (5.2)	25(19.4)	56(13.8)
Enterobacter	20(3.8)	1(0.8)	5(1.2)
E. faecalis	19(3.6)	9(7)	9(2.2)
S. Marcescens	19(3.6)	2(1.5)	5(1.2)
Total	521	129	406

UCI, intensive care unit; CoNS, coagulase negative staphylococcus

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A brief communication is focused in a single subject, which should be concise and a new point of view presentation of the subject. The scope of this section is intended to be wide and methods, results and discussion should be in the same text. A brief communication should contain:

- An abstract of no more than 200 words;
- No more than 4 keywords;
- Text should not exceed 12 double-spaced typed pages of 23 lines each;
- A maximum of 2 figures or tables (or one of each);
- No more than 20 references;
- The text should not be divided into separate sections;
- Authors should state in the cover letter that the manuscript is intended to be a brief communication;
- Number of authors should not exceed 5.

Review article

This section is for an updated presentation on a specific topic. This section should contain critical analysis and a new point of view of a relevant area and not a chronological description of the literature. This section aims to raise discussion among readers about controversial issues and the development of concepts in Infectious Diseases. A review article has to bring the new point of view of the focus of the subject. A minireview is focused on a restricted part of a subject. A minireview and review article should contain:

- An abstract of no more than 300 words;
- No more than 7 keywords;
- No more than 80 references;
- The text may be divided into sections with appropriate titles and subtitles;
- Number of authors should not exceed 5;
- Authors should state in the cover letter that the manuscript is intended to be a review or mini review article.

Case reports

Reports of clinical cases must contain a brief introduction about the nature of the case diagnosis, whose focus is the importance of the subject. The case has to be described with data and reports of examinations, treatment and prognosis of the case, discussion about the importance of the findings and presentation of the case in relation to literature. A case report should have a special interest to the clinical research community or it has to be a rare case; or to present a new diagnostic method; or new or modified treatment. A case report article should contain:

- An abstract of no more than 150 words;
- No more than 4 keywords;
- No more than 20 references;
- The text may be divided into sections: brief introduction with a review of literature, case reports, and conclusion;
- Number of authors should not exceed 5;
- Authors should state in the cover letter that the manuscript is intended to be a case report article.

Clinical infectious diseases images

For submission to Clinical Infectious Diseases Images, which is not intended as a vehicle for case reports, all text should contain:

- A minimum of references (no more than 4);
- No abstract;
- The text should be uniform and contain no more than 300 words;
- Number of authors should not exceed 5.

Letters to the editor

Letters may be written in response to previous content published in The Brazilian Journal of Infectious Diseases (BJID) or on any topic of general interest or concern. In the first case, the letter must emphasize the main message of the author of the article, focusing the contribution of that scientific article in the medical practice, drawing attention to the reference and impact it had on the community. The Letter to the Editor should contain:

- Title and the text with no more than 23 line pages;
- No more than 5 references;
- Number of authors should not exceed 5.

MANUSCRIPT FORMATS

Cover letter

For all manuscripts, authors must indicate in a cover letter:

- Title of article;
- Name(s) of all author(s);
- Address, telephone number, fax, and e-mail of the corresponding author;
- A statement signed by the corresponding author confirming that the manuscript content represents the views of the coauthors, that neither the corresponding author nor the coauthors have submitted duplicate or overlapping manuscripts elsewhere, and that the items indicated as personal communications in the text are supported by the referenced person;
- The registration number of all randomized controlled trials and clinical trials, in accordance with the International Committee of Medical Journal Editors;
- In the same case, the corresponding author has to send a statement indicating that written informed consent was obtained from all participants;
- All original articles should indicate the number of the Ethics Committee approval. If the article does not require an approval from the Ethics Committee, the author should write it separately in the article;
- Animal experimentation should be carried out according to institutional guidelines for experimental use of animals;
- The authors should obtain written permission to reproduce figures and tables from other sources;
- If the study was supported by any institution, it has to be indicated in the cover letter.

The cover letter should be in one double-spaced electronic document, title (no more than eight words in the title); no more than five (or ten, when an original article) authors may be listed, including name, institution, address, email address, telephone and fax number of each author; the text should contain no more than 300 words.

Supplements to the BJID include articles under a unifying theme, such as those summarizing presentations of symposia or focusing on a specific pathogenic process or antimicrobial agent. These will be added to the regular bimonthly publication as appropriate, and will be peer reviewed in the same manner as submitted manuscripts.

For each manuscript a registration number will be assigned and the author will be notified that the manuscript is complete and adequate to start the review process.

Format of articles and letters

Contributions should be double-spaced and written in English. All manuscripts are to be typed double-spaced, including text, tables, references and legends; the character should be Time New Roman for all text, including figures, graphics and tables, and the tool "insert > symbol" for Greek character; size 12 should be used in all manuscript. The manuscripts have to be saved in Word document and the figures should be saved in CorelDraw, JPG or TIF document with high resolution - minimum of 300 dpi.

Use of digital resources

Manuscript, Title Page, Cover Letter, and Author Agreement files in DOC format (Winword); bars or lines figures in XLS (Excell standard); photos and figures, with minimum resolution of 300 dpi, in JPG format. Please do not attach titles and letterings to illustrations. Please do not insert illustrations on text. Each illustration shall have an individual file. File name shall express illustration type and numbering (Figure 1, Table 2, for example). Illustration titles and letterings duly numbered shall be in separate text file. Copies or reproductions of other publications will be allowed only with the attachment of express authorization of the Editing company or the author of the original article.

Titles and subtitles

- Titles should be in bold;
- Subtitles should be in underscore;
- Titles should not have abbreviations or acronyms;
- Titles should not exceed two printed lines;
- Do not exceed 80 characters (inc. spaces).

Author affiliations

- Complete name of the authors (do not abbreviate);
- Affiliations of all authors;
- Name, mailing addresses, phone and fax number, e-mail, state, city and country of the corresponding author;
- Acknowledgement of research grants and fellowships (agency and grant number).

Keywords

- Consider the manuscript formats to verify the number of keywords;
- Use capital letter for the first word, the other should be in regular form.

Abstract

- The abstract should briefly contain the objective, data, methods, results and discussion of the study or presentation to ensure the reader's understanding of the manuscript;
- Do not use abbreviations in abstract;
- Do not use references in abstract;
- Consider the manuscript formats to verify the number of words.

Introduction

- In the text of Introduction the authors have to reveal the aim of the study, the purpose of the research, and the basic literature about the subject.

Material and methods

- This section should be subdivided by short underscore headings referring to methods used;
- This section cannot contain figures or tables;
- The material and methods used must be carefully described to allow the study repetition and to determine if the results were possible and correct;
- Papers with statistical testing should state the name of the test, the name for each analysis, the comparisons of interest, a justification of that test, the alpha level for all tests, whether the tests were over two-tailes, and the actual p-value for each test;
- Data sets should be summarized with descriptive statistics, which should include then for each data set, a clearly labeled measure of centre (such as the mean or median), and a clearly labeled measure of variability (such as the standard deviation or range).

Results

- The data of the results should be described concisely;
- Tables, graphics and figures have to be inserted in this section;
- The data presented in this section have to be oriented by universal units;
- Tables should be clear enough to the readers do not need the text to understand them;
- Tables should be presented on separate pages, portrait orientation, and upright on the page;
- Tables should present a short one-line title in bold;
- Tables have to be numbered consecutively with Arabic numerals in the text;
- Symbols and abbreviations are defined immediately below the table;
- More information about the table should be below the symbols and abbreviations;
- If the table is from another source, the authors must indicate the source and send the permission to the Journal.

Figures/Graphics

- Figure legend should be listed one after the other, as a part of the text document, separate from the figure files, with a short one-line title in bold.
- Figures should be submitted in CDR, TIF, JPG file (300 dpi);
- Figures should be clear enough that the readers do not need the text to understand them;
- Figures should be presented on separate pages, portrait orientation, and upright on the page;
- Figures have to be numbered consecutively with Arabic numerals in the text;
- Symbols and abbreviations are defined immediately below the figure, as well as any other informations about the figures;
- If the figure is from another source, the authors must indicate the source and send the permission to the Journal.

Discussion

- The discussion presents the results comparing and evaluating them to literature and the existing knowledge. References to other studies should appear in the Discussion to compare the data obtained in the methods and results of the paper.

Acknowledgements

- Authors can thank anyone who helped them do the work or study.

Finnancial support

- The authors must indicate in the cover letter if the study was supported by institutions.

Abbreviations and symbols

- All abbreviations have to be explained in the text, figure and table legends when they first appear;
- Include the abbreviation in parenthesis after they first appeareance.
- Abbreviate units [(5 mL, not 5 milliliters (mL)];
- Do not abbreviate institutions;
- Abbreviations must follow the format of the National Library of Medicine (USA) as in Index Medicus.

Units

- Follow the use of the The International System of Units (SI) (http://physics.nist.gov/cuu/Units).

References

- They should go in the final part of the article, according to the quotation order in the text, in which should appear the Arabic numerals superscripted. Please quote all the authors in works with until six authors; after six authors, quote the first three followed by the expression et al. Reference Manager or Endnote programs are strongly recommended for use adopting the "Vancouver" style.

Examples for reference citation are presented below. Authors should consult NLM's Citing Medicine for additional information on the reference formats.

Article

Turner SW, Young S, Goldblatt J, Landau LI, Le Souëf PN. Child hood asthma and increased airway responsiveness a relationship that begins in infancy. Am J Respir Crit Care Med. 2009;179:98-104.

Chang ML, Yang CW, Chen JC, et al. Disproportional exaggerated arpartate transaminase is a useful prognostic parameter in late leptospirosis. World J Gastroenterol. 2005;11:5553-6.

Book chapter

Taylor DM, Personnet J. Epidemiology and natural history of Helicobacter pylori infection. In: Blaser MJ, Smith PD, Ravdin J eds. Infections of the gastrointestinal tract. New York: Raven Press, 1994.

Book

Polak JM, Van Noordan S. An introduction to immunochemistry: current techniques and problems. Oxford, UK: Oxford University Press, 1987.

Abstract

Blatt SP, Butzin CA, Lucey DR, Melcher GP, Hendrix CR. Anergy status and CD4 CD29 memory T-cells predict progression to AIDS (abstract PoB 3480). In: Program and abstracts: VIII International Conference on AIDS (Amsterdam). Amsterdam: CONGREX Holland, 1992.

SCOPE AND POLICY

The aim of BJID is to be relevant in the broadest sense to all aspects of Infectious Diseases and its fields. The manuscripts submitted to BJID should develop new concepts or experimental approaches; they have to describe new principles or improve-

ment of an existing method and their results; they have to bring new data about a subject which will be important to physichians; so they could not be a single presentation of known data.

PUBLICATION ETHICS

- All the listed authors have to agree on all contents (authors must approve the article galley proof) and they are responsible for all informations included in the text.
- The corresponding author is responsible for all communications between the Journal and all coauthors, before and after publication.
- The corresponding author has to make a statement confirming that the content of the manuscript represents the views of the coauthors, that neither the corresponding author nor the coauthors have submitted duplicate or overlapping manuscripts elsewhere, and that the items indicated as personal communications in the text are supported by the referenced person.
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- The editors of BJID may seek advice about submitted papers not only from technical reviewers but also on any aspect of a paper that raises concerns. These may include, for example, ethical issues or issues of data or materials access.
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The Journal editors treat the submitted manuscript and all communication with the authors as confidential between themselves and the peer-reviewers. Similarly, authors must treat communication with the Journal as confidential.

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BJID is a peer-review Journal, so all papers (except Letters to the Editor) are evaluated by this system. If the paper follows the scope of the Journal, it will be sent to two or three independent reviewers, selected by the editors (two from the editorial board and one any other expertise).

Authors may suggest appropriate consultants for review of the manuscript, but these suggestions may not be followed.

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The review process will ordinarily require two months.

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General information

The reviewers will be invited by the editor of BJID to do the comments about an article, in accordance with the specialty of each referee. Questions about a specific manuscript should be directed to the editor who is handling the manuscript.

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All submitted manuscripts are read by the editorial staff. To save time for authors and peer-reviewers, only those papers that seem most likely to meet our editorial criteria are sent for formal review. Those papers judged by the editors to be of insufficient general interest or otherwise inappropriate are rejected promptly without external review (although these decisions may be based on informal advice from specialists in the field).

Manuscripts judged to be of potential interest to our readership are sent for formal review, typically to two or three reviewers, but sometimes more if special advice is needed (for example on statistics or a particular technique). The editors then make a decision based on the reviewers' advice, from among several possibilities:

- Accept, with minor corrections;
- Invite the authors to revise their manuscript to address specific concerns before a final decision is reached;
- Reject, but indicate to the authors that further work might justify a resubmission;
- Reject outright, typically on grounds of specialist interest, lack of novelty, insufficient conceptual advance or major technical and/or interpretational problems.

LEGAL AND ETHICAL CONSIDERATIONS

According to the Uniform Requirements for Manuscripts Submitted to Biomedical Journals (International Committee of Medical Journal Editors - February 2006).

Conflict of interest

Public trust in the peer review process and the credibility of published articles depend in part on how well conflict of interest is handled during writing, peer review, and editorial decision making. Conflict of interest exists when an author (or the author's institution), reviewer, or editor has financial or personal relationships that inappropriately influence (bias) his or her actions (such relationships are also known as dual commitments, competing interests, or competing loyalties). These relationships vary from those with negligible potential to those with great potential to influence judgment, and not all relationships represent true conflict of interest. The potential for conflict of interest can exist whether or not an individual believes that the relationship affects his or her scientific judgment. Financial relationships (such as employment, consultancies, stock ownership, honoraria, paid expert testimony) are the most easily identifiable conflicts of interest and the most likely to undermine the credibility of the journal, the authors, and of science itself. However, conflicts can occur for other reasons, such as personal relationships, academic competition, and intellectual passion.

Informed consent

Patients have a right to privacy that should not be infringed without informed consent. Identifying information, including patients' names, initials, or hospital numbers, should not be published in written descriptions, photographs, and pedigrees unless the information is essential for scientific purposes and the patient (or parent or guardian) gives written informed consent for publication. Informed consent for this purpose requires that a patient who is identifiable be shown the manuscript to be published. Authors should identify individuals who provide writing assistance and disclose the funding source for this assistance. Identifying details should be omitted if they are not essential.

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Clinical trials registry

Clinical trials must be registered according to WHO recommendation at www.who.int/ictrp/en/. The definition of clinical trial include preliminary trials (phase I): any study with prospective recruiting of subjects to undergo any health-related intervention (drugs, surgical procedures, equipment, behavioral therapies, food regimen, changes in health care) to evaluate the effects on clinical outcomes (any biomedical or health-related parameter, including pharmacokinetics measurements and adverse reactions).

The Journal has the right not to publish trials not complying with these and other legal and ethical standards determined by international guidelines.