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ORIGINAL

Microbiological profile of infections in the Intensive Care Units of Colombia (EPISEPSIS Colombia)

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Abstract
Background and objective: Valid and reliable data regarding sepsis is lacking in Colombia. Our aim was to determine the prevalence of the microorganisms in the main infections treated in Intensive Care Units (ICUs) in our country.
Methods: This is a sub-study of a prospective cohort with 10 general hospitals in Colombia during a 6-month period. The inclusion criteria were hospitalization in ICU and confirmation of infection according to the CDC definitions. Patients were classified into three groups, that is, community, hospital and intensive care, according to the site where the infection was acquired.
Results: A total of 826 patients were included in this analysis. Of these, 51% developed infections in the community, 5.33% in the hospital and 43.7% in intensive care unit. Overall, the most common diagnoses were pneumonia (29.54%), intra-abdominal infection (18.16%) and urinary tract infection (11.62%). The most frequent germ in community-acquired infections was *E coli* –lung (16. 4%), peritoneum (57.7%), urine (55.5%), blood (22.4%)–. *E Coli*–peritoneum (29.3%), urine (52.9%)– also predominated in the ICU-acquired infections, except for lung and blood in

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which *Staphylococcus aureus* (32.4%) and *Klebsiella pneumoniae* (15.7%) were the most prevalent. Cultures were requested from 655 patients, 40% of them having received antibiotics before cultures were taken, although this did not affected the percentages of positive cultures (P = 0.583).
Conclusions: Pneumonia was the main cause of infection regardless of the site of acquisition. *E. coli* was the most prevalent germ, except in the pulmonary infections acquired in UCI in which *S. aureus* was the most prevalent.

PALABRAS CLAVE
Infección;
Sepsis;
Microbiología;
Epidemiología;
Unidad de cuidados intensivos

Perfil microbiológico de las Infecciones en Unidades de Cuidados Intensivos de Colombia (EPISEPSIS Colombia)

Resumen
Introducción y objetivo: En Colombia faltan datos fiables sobre el comportamiento de la sepsis. Se pretende determinar la prevalencia de los microorganismos en las principales infecciones tratadas en las unidades de cuidados intensivos (UCI) de nuestro país.
Métodos: Este es un subestudio de una cohorte prospectiva recolectada en 10 hospitales durante 6 meses. Los criterios de inclusión eran hospitalización en UCI y confirmación de una infección según las definiciones del CDC, considerando tres grupos (comunidad, hospital, UCI) según el sitio de adquisición de la infección.
Resultados: Se incluyó en el análisis a 826 pacientes; el 51% contrajeron procesos infecciosos extrahospitalarios; el 5,33%, en el hospital y el 43,7%, en UCI. Los diagnósticos más frecuentes fueron neumonía (29,54%), infección intraabdominal (18,16%) e infección del tracto urinario (11,62%). El microorganismo más frecuente en las infecciones extrahospitalarias fue *Escherichia coli* –pulmón (16,4%), peritoneo (57,7%), orina (55,5%) y sangre (22,4%)–. En las adquiridas en UCI predomina también *E. coli* –peritoneo (29,3%) y orina (52,9%)–, excepto en pulmón y sangre, en los que fueron *Staphylococcus aureus* (32,4%) y *Klebsiella pneumoniae* (15,7%) los más prevalentes. Se tomaron cultivos a 655 pacientes, de los que el 40% recibió antibióticos antes de la toma, sin que esto afectara al porcentaje de positividad (p = 0,583).
Conclusiones: La neumonía fue la infección más frecuente independientemente del sitio de adquisición. *E. coli* fue el patógeno más prevalente, excepto en las infecciones pulmonares adquiridas en UCI, donde lo fue *S. aureus*.

Introduction

Sepsis is established from the clinical suspicion of infection with evidence of a systemic inflammatory response as defined by one or more of the following criteria: fever or hypothermia, leukocytosis or leukopenia, tachycardia and tachypnea.

The epidemiology of sepsis varies among different regions: in the United States, in the period between 1979 and 2000 there was an annual rise in the incidence of sepsis of 8.7%, implying an increase from 164,000 cases (82.7/100,000 inhabitants) to almost 660,000 cases (240.4/100,000 inhabitants), with a lowering of in-hospital mortality from 27.8% to 17.9%.[3] In France, a registry of 22 hospitals over an 8-year period (1993-2000) likewise found the incidence of septic shock to have increased from 8.2/100 admissions in 1993 to 9.7/100 admissions in 2000.[4]

Infections in Intensive Care Units (ICU) are caused by multiresistant microorganisms, affecting over 20% of all patients and giving rise to a mortality rate of over 30%,[5] with the generation of important management costs.[6] Out-hospital infections also exhibit microbiological high resistance profiles.[7]

The EPIC II study, which evaluated 14,414 patients in 1265 ICUs of 75 countries, found 51% of the patients to be infected, and 71% of these subjects were receiving antibiotics. The most frequent infections were of respiratory origin (64%); the cultures proved positive in 70% of the cases, gramnegative microorganisms were isolated in 62%, grampositive microorganisms in 47%, and fungi in 19%.[8]

A literature review of the epidemiology of septicemia in Latin America found the published studies to be extremely heterogeneous in terms of design, study population, sample size, endpoints and follow-up. The studies even differed in terms of their definition of sepsis, thus making it impossible to gain a precise idea of the magnitude of the problem in Latin America.[9] To our knowledge, the only study in this geographical setting referred to the epidemiology of sepsis in Intensive Care was carried out in Brazil.[10] In a series of 1383 patients, the observed rates of sepsis, severe sepsis and septic shock were 61.4, 35.6 and 30/1000 days/patient, respectively –the main site of infection being the respiratory

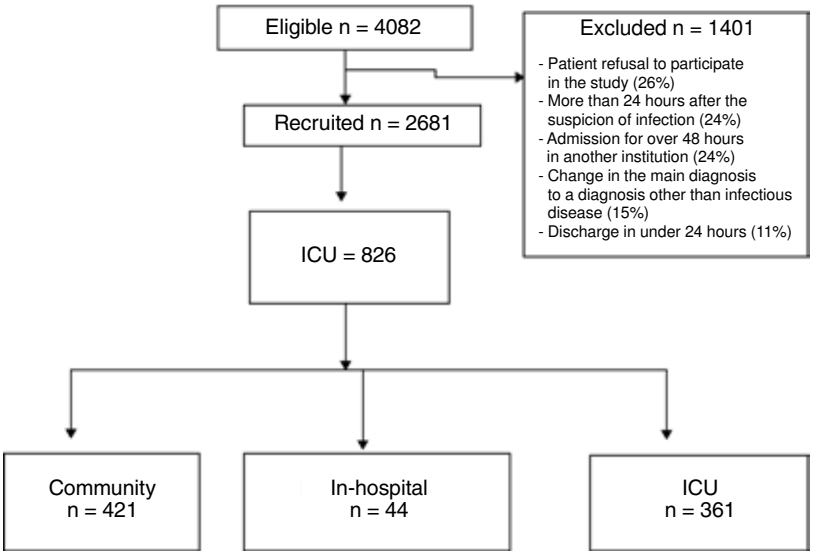

Figure 1 Study population.

tract. However, no analyses were made of the corresponding microbiological profiles.

In Colombia there are presently three groups (GREBO, GRUVECO and CIDEIM) in charge of the vigilance of microbiological isolates in different hospitals throughout the country, with no direct correlation to the infections profile found in Intensive Care.

We therefore designed a multicenter study to describe the prevalence of the microorganisms present in the most common infections found in ICUs, the types of cultures requested and their positivity in relation to the prior start of antibiotic treatment.

Material and methods

Patients

A prospective, multicenter cohort study was carried out involving patients admitted to 10 hospitals in four main cities in Colombia, between 1 September 2007 and 29 February 2008. The eligible patients were over 18 years of age and presented one of the following three criteria: a probable or confirmed diagnosis of infection as established from the clinical data; changes in body temperature (> 38 or < 36 °C); or hypotension in the absence of a specific cause, with admission to the Emergency Department, ICU or hospital. As definitive inclusion criterion, the patients were required to present infection complying with the definition based on the criteria of the Centers for Disease Control (CDC).[11] The present study is a sub-study including only those patients admitted to Intensive Care, and stratified according to whether the infection was of an out-hospital nature, nosocomial (in-hospital, or occurred in the ICU.

The exclusion criteria were: patient refusal to participate in the study, eligibility evaluation more than 24 hours after the suspicion of infection, admission for over 48 hours in another institution immediately before current hospitalization, the non-availability of follow-up for 28 days, discharge in under 24 hours, and a change in the main diagnosis to a diagnosis other than infectious disease during hospitalization.

The study protocol was approved by a review board in each center. Informed consent was obtained in two hospitals, while in the rest of the centers consent was not obtained on the grounds that this is an observational study.

Institutions

Ten general and university hospitals in four cities of Colombia were invited to participate on the basis of their geographical importance in each region. The hospitals were located in Bogotá: Fundación Cardio-Infantil (153 adult beds, 46 Intensive Care (IC) beds), Hospital Universitario San Ignacio (241 adult beds, 32 IC), Hospital Santa Clara (108 adult beds, 15 IC); in Cali: Fundación Valle del Lili (232 adult beds, 40 IC) and Hospital Universitario del Valle (585 adult beds, 48 IC); in Cartagena: Clínica Madre Bernarda (100 adult beds, 11 IC) and Hospital de Bocagrande (75 adult beds, 19 IC); and in Medellín: Hospital Pablo Tobón Uribe (300 adult beds, 18 IC), Clínica Universitaria Bolivariana (149 adult beds, 12 IC) and Hospital Universitario San Vicente de Paúl (625 adult beds, 32 IC). This latter hospital moreover served as coordinating center.

Data collection, evaluation and quality control

One or two nurses were trained, depending on the number of beds in each hospital, in two working sessions of two days each. A pilot study was carried out during three months, immediately before the start of recruitment. In each hospital there was also a co-investigating physician in charge of reviewing data precision and consistency, as well as the diagnosis of each patient. In addition, each case report form was evaluated and reviewed weekly, based on a double-input form, in the data coordinating center of the University

Table 1 Distribution of demographic variables and the severity of infection, according to the place where infection occurred among the patients admitted to Intensive Care in Colombia over a 6-month period during the year 2007

Origin	Age (years), mean	Sex, %		SOFA score, mean ± SD	APACHE II score, mean ± SD
		Males	Females		
Out-hospital	56.23	51.78	48.22	6.34 ± 3.42	16.24 ± 6.82
ICU	52.1	52.91	47.09	6.48 ± 3.7	13.69 ± 6.41
In-hospital	58.28	56.82	43.18	6.34 ± 4.41	15.3 ± 6.57
General	54.53	52.54	47.46	6.08 ± 3.48	15.08 ± 6.74

of Antioquia. Any incoherence, imprecision or loss of data implied returning the form to the co-investigator in charge for due correction in the week after review of the data in the coordinating center. An evaluation was also made by one of the main co-investigators in each hospital during the first month of the study.

The severity of the disease was assessed based on the APACHE II score (Acute Physiologic and Chronic Health Evaluation II),[12] and the magnitude of organ dysfunction was measured with the SOFA score (Sequential Organ Failure Assessment).[13] Both scales were applied within the first 24 hours after inclusion of the patient. We also collected data relating to the patient demographic characteristics, diagnosis of the infection, type of cultures with the corresponding microbiological report and antibiogram during the first 7 days after inclusion of the patient, and the start or not of antibiotic treatment before sampling for culture.

Study results

The study was designed to describe the prevalence of the microorganisms involved in out-hospital, nosocomial and ICU infectious processes, the types of cultures requested and their positivity in relation to the prior start of antibiotic treatment.

Statistical analysis

The results for the variables exhibiting a normal distribution were reported as the mean ± standard deviation (SD) and interquartile range, or as proportions with the corresponding 95% confidence interval (CI). Comparisons between continuous variables were made using the Student t-test in the presence of a normal distribution, and with the Mann-Whitney U-test for variables with a non-normal distribution. The categorical variables in turn were analyzed with the chi-squared test, except in those cases involving a small sample size and where the Fisher exact test proved necessary. Statistical significance was considered for $p < 0.05$.

Results

Over a period of 6 months, 4082 patients in hospital admission, the Emergency Department and ICU proved eligible for inclusion in the study. Of these subjects, 1401 were excluded and 2681 were included. In relation to the latter, 826 (30.8%) were in the ICU and so were subjected to analysis to the effects of the present study. The distribution according to where infection occurred was as follows: out-hospital 421 (50.97%); in-hospital 44 (5.33%), and in the ICU 361 (43.7%) (Fig. 1).

The mean patient age was 54.5 ± 20.3 years, with an almost equal distribution between males and females (1:1.1). The mean SOFA and APACHE II scores were 6.08 ± 3.48 and 15 ± 6.74, respectively. The distribution of these data according to the place where infection occurred is shown in Table 1.

The most frequent infections among the general population were of respiratory origin (29.54%; nosocomial, 17.07%; out-hospital, 12.47%). In all groups the three

Table 2 Prevalence of the main infections in the ICUs of Colombia according to the place where infection occurred

Type of infection	Out-hospital	ICU	In-hospital	General
Intraabdominal infection	84 (19.95)	63 (17.45)	3 (6.82)	150 (18.16)
Nosocomial pneumonia	–	119 (32.96)	21 (47.73)	140 (17.07)
Out-hospital pneumonia	102 (24.23)	–	–	102 (12.47)
Symptomatic urinary tract infection	53 (13.06)	40 (11.08)	1 (2.27)	94 (11.62)
Clinical sepsis	35 (8.31)	40 (11.08)	2 (4.55)	77 (9.32)
Soft tissue infections	47 (11.16)	11 (3.05)	2 (4.55)	60 (7.26)
Hematological infections	17 (4.04)	33 (9.14)	1 (2.27)	51 (6.17)
Catheter-related urinary tract infection	4 (0.95)	16 (4.43)	4 (9.09)	24 (2.91)
Endometritis	2 (0.48)	1 (0.28)	2 (4.55)	5 (0.61)
Others	77 (18.3)	55 (15.24)	10 (2.72)	142 (15.02)

The data are expressed as n (%).

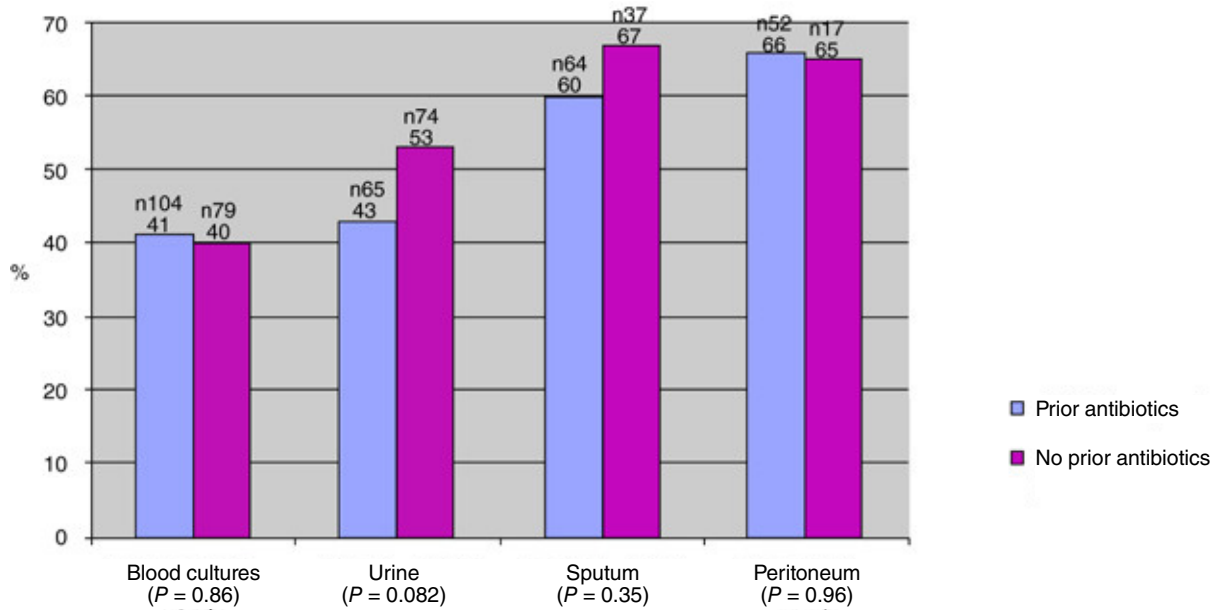

Figure 2 Percentage positive results in the different cultures, considering prior antibiotic use.

most common infections were pneumonia, intraabdominal infection and urinary infection. The groups in turn different in relation to the fourth most common cause of infection: in the out-hospital cases soft tissue infections were the most common forms, versus endometritis in the in-hospital subject, and catheter-related bacteremia in the ICU (Table 2).

Cultures were obtained from 655 patients (79.1%); of these, 60% were obtained before the start of antibiotic treatment. The start of antibiotics before or after the collection of samples did not influence positivity in any of them (Fig. 2).

The most frequently requested samples corresponded to blood samples for culture (obtained in 54.4% of the patients), followed by urine (35.1%), sputum (19.6%), peritoneal fluid (12.71%), other exudates (4.8%), cerebrospinal fluid (CSF) (4.2%), skin and soft tissues (3.8%), pleural fluid (2.06%) and joint fluid (0.5%).

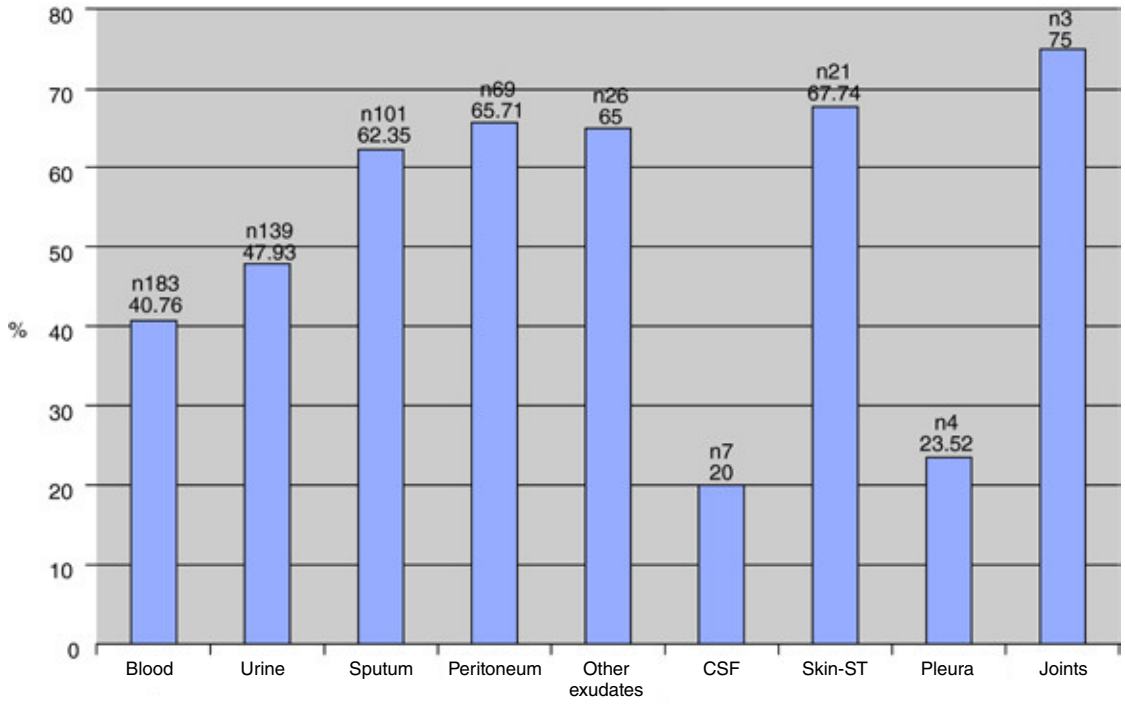

Figure 3 Percentage of positive results in the different cultures obtained from the patients admitted to Intensive Care (CSF: cerebrospinal fluid, Skin-ST: skin and soft tissues).

On evaluating percentage positivity of the requested samples, those corresponding to joint fluid, skin and soft tissues and peritoneal fluid yielded the highest rates, while CSF, pleural fluid and blood cultures showed the lowest percentage positivities (Fig. 3).

In the blood cultures reported as being positive, grampositive species were isolated in 43.5% of the cases, gramnegative species in 54.5% and fungi in 2%. The samples obtained from patients with out-hospital infections proved positive in 36.1% of the cases, and the most frequently reported microorganism was *Escherichia coli*. In turn, 40.9% of the blood cultures obtained from in-hospital patients proved positive; of these cases, 88.8% corresponded to gramnegative bacilli, with no predominant microorganism. In the ICU, 46.35% of the blood cultures proved positive, and the most frequently isolated organism in this case was *Klebsiella pneumoniae*.

Samples were obtained from 105 (70%) of the patients with abdominal infections, yielding 69 positive cultures (65.71%)(with positivity in 57.6% of the out-hospital cases, 74.48% of the ICU infections and 100% of the in-hospital cases). The two most commonly isolated microorganisms in the out-hospital and nosocomial (ICU and in-hospital) infections were *E. coli* and *K. pneumoniae*.

Samples in turn were obtained from 162 (66.3%) of the patients with pneumonia, yielding 101 positive cultures (62.34%) (with positivity in 55.21% of the out-hospital cases, 75% of the in-hospital infections and 64.84% of the ICU infections). The most frequently isolated microorganisms according to the place where infection occurred were *E. coli* in the out-hospital cases, and methicillin-sensitive *Staphylococcus aureus* (MSSA) in the in-hospital infections. In the case of ICU-acquired pneumonia, and although 62.1% of the isolates corresponded to gramnegative bacilli, the most frequently isolated pathogen was *S. aureus*.

Of the 129 patients diagnosed with urinary tract infection, urine cultures were requested in 118 cases (91%), with positive results in 83%. The most frequently isolated microorganism in each of the subgroups was *E. coli*.

The microorganisms most frequently isolated from the different samples are shown in Table 3.

Table 3 Frequency of microorganisms according to the type of sample and place where infection occurred

	Out-hospital	n (%)	ICU	n (%)	In-hospital	n (%)
Blood	*Escherichia coli*	19 (22.4)	*Klebsiella pneumoniae*	14 (15.7)	*Enterobacter cloacae*	2 (22.2)
	Klebsiella pneumoniae	13 (15.3)	*Staphylococcus aureus*	12 (13.5)	*Escherichia coli*	1 (11)
	Staphylococcus aureus	8 (9.4)	*Escherichia coli*	8 (9)	*Klebsiella pneumoniae*	1 (11
	Streptococcus pneumoniae	4 (4.7)	*Staphylococcus epidermidis*	7 (7.9)	*Pseudomonas aeruginosa*	1 (11)
Urine	*Escherichia coli*	35 (55.5)	*Escherichia coli*	36 (52.9)	*Escherichia coli*	3 (37.5)
	Klebsiella pneumoniae	8 (12.7)	*Enterobacter cloacae*	5 (7.3)	*Klebsiella pneumoniae*	2 (25)
	Proteus mirabilis	5 (7.9)	*Enterococcus faecalis*	4 (5.9)	*Proteus mirabilis*	1 (12.5)
	Enterococcus faecalis	2 (3.2)	*Pseudomonas aeruginosa*	3 (4.4)	*Pseudomonas aeruginosa*	1 (12.5)
Bronchial secretion	*Escherichia coli*	4 (16.7)	*Staphylococcus aureus*	24 (32.4)	*Staphylococcus aureus*	3 (66.7)
	Klebsiella pneumoniae	3 (12.5)	*Klebsiella pneumoniae*	13 (17.6)	*Streptococcus viridans*	1 (33.3)
	Staphylococcus aureus	3 (12.5)	*Pseudomonas aeruginosa*	11 (14.9)		
	Streptococcus pneumoniae	2 (8.3)	*Escherichia coli*	6 (8.1)		
	Pseudomonas aeruginosa	2 (8.3)	*Enterobacter cloacae*	3 (4)		
Peritoneal fluid	*Escherichia coli*	15 (57.7)	*Escherichia coli*	12 (29.3)	*Klebsiella pneumoniae*	2 (100)
	Klebsiella pneumoniae	3 (11.5)	*Klebsiella pneumonia*	5 (12.2)		
	Bacillus sp.	2 (7.7)	*Acinetobacter baumannii*	4 (9.7)		
	Pseudomonas aeruginosa	1 (3.8)	*Pseudomonas aeruginosa*	3 (7.3)		

Discussion

In this first study carried out in Colombia on the microbiological profile of the main infections seen in Intensive Care, respiratory infection was found to be the main cause of admission, in coincidence with the rest of the published series[10,14-25] - with the exception of the works of Cheng et al.[26] and Degoricija et al.,[27] in which abdominal infections and urinary infections were the most prevalent, respectively.

Three studies[16,17,25] have described the infections according to the place in which infection occurred. In this context, lung infections were found to be the most common infections both out-hospital and in-hospital, in coincidence with our own observations.

Seven of the studies[17-19,21,24,25,27] differentiated the infections according to the place in which infection occurred, and in most cases out-hospital infections were the processes most often determining admission to Intensive

Table 4 Comparison of the different series according to general data of the infections in Intensive Care

	Tanriover et al.[16]	Alberti et al.[17]	Engel et al.[18]	Zahorec et al.[19]	Karlsson et al.[21]	Vincent et al.[24]	Khwannimit et al.[25]	Degoricija et al.[27]
Admission criteria	Sepsis	SIRS, sepsis, severe sepsis and septic shock	SIRS, sepsis, severe sepsis and septic shock	Severe sepsis	Severe sepsis	SIRS, sepsis, severe sepsis and septic shock	Severe sepsis	Sepsis
Population size	63	14,364	1348	121	470	1177	390	314
APACHE score			19 (13-24)		24.1 ± 9		26.8 ± 9.4	19.98 ± 7.8
SOFA score			8 (5-11)	9.93		5.6 ± 3.7		5.82 ± 3.35
Place of occurrence	Community 50% Nosocomial 50%	Community 56.4% Nosocomial 43.6%	Community 39.1% ICU 32.9% Nosocomial 13.8%	Nosocomial 50.4% Community 27.7% ICU 19% Unknown 3.3%	Community 58.3% Nosocomial 39%	Outside ICU 76.3% ICU 23.7%	Nosocomial 55.6 Community 44.4	Community 72.3% Nosocomial 27.7%
Positivity of the cultures, %	47.7	Nosocomial 70.6 Community 54.8%	45.4		40.1	60		74.8
Origin of sepsis	Community: Pneumonia 38.2% Abdomen 23.5% Urinary 11.8% Skin and soft tissues 11.8% Nosocomial Pneumonia 50% Skin and soft tissues 14.7% Urine 14.7% Abdomen 10.6%	Community: Pneumonia 44% Urinary 7.2% Abdomen 7.2% Bacteremia 5.8% Nosocomial Pneumonia 37.3% Abdomen 13.2% Bacteremia 11.3% Urinary 8.2% ICU Pneumonia 41.7% Bacteremia 15.3% Urinary 12.6% Abdomen 8.5%	Lung 62.9% Abdomen 25.3% Skin 8.7% Urinary 6.5%	Lung 53.4% Abdomen 31.4% Urine 19% Surgical wound 16.5%	Lung 43% Abdomen 32% Skin or surgical wound 10% Urine 5%	Lung 68% Abdomen 22% Blood 20% Urine 14%	Community: Pneumonia 44.5% Abdomen 19% Urinary 6.9% Bacteremia 6.3% Nosocomial Pneumonia 54.4% Abdomen 16.6% Bacteremia 6.9% Skin and soft tissues 5.5%	Urine 53.5% Skin 18.5% Blood 19.8% Lung 15.6%

SIRS: systemic inflammatory response syndrome.

Care, with the exception of the series from Thailand[25] and Slovakia,[19] where nosocomial infections were the most prevalent cause (55.6 and 69.4% respectively). In our study there were no true differences between the out-hospital infections (50.97%) and the nosocomial infections (49.03%). Table 4 compares the different aforementioned studies in terms of the epidemiological characteristics, severity and origin of the infectious process.

The percentage distribution of the microbiological identification of the cultures was characterized, including consideration of the type of culture carried out. A number of studies have also reported on culture positivity,[14,15,18,21,24,27] though most of them are limited to blood cultures, with variable percentages of positivity between 35-75%. This coincides with our own findings, where the blood culture positivity rate was 40.9%. None of these studies examined the relationship between the frequencies of the different microbiological isolates and the prior start of antibiotic treatment. In our series the use of antibiotics before or after sampling did not influence the corresponding positivity findings. However, no evaluation was made of the possible existence of a relationship between sample positivity and the presence or absence of resistance to the antibiotic treatment on the part of the isolated microorganism, or of the time elapsed from the start of antibiotic treatment to the moment of sample collection. As a result, it cannot be concluded whether it is irrelevant to administer or not administer antibiotics prior to sample collection.

In this study, *E. coli* predominated in the samples corresponding to the out-hospital infections (bronchial secretions, peritoneal fluid, urine and blood). In the nosocomial infections the predominant species again was *E. coli* in urine and peritoneal fluid, while *K. pneumoniae* and *S. aureus* respectively predominated in blood and lung. Similar data have been reported by the Turkish series.[16] The findings vary from one country to another. As an example, in the study from Thailand[25] *Mycobacterium tuberculosis* was the most frequent microorganism in out-hospital pulmonary infections, while in the nosocomial infections *E. coli* was seen to predominate in the urine and peritoneal fluid samples - *Acinetobacter, Klebsiella* and *Pseudomonas* in turn predominating in the lungs. This points to the need for local, regional and global vigilance systems as an integral part of infection prevention and control programs, with a view to facilitating the information required to modify the antibiotic prescription protocols and design new interventions for the control of microbial resistances.

The strong points of our study include the following: a) the patients were definitively included in the study only if infection was confirmed according to the criteria of the CDC,[11] thereby affording high specificity regarding the diagnostic criterion; b) culture positivity was related to the prior start of antibiotic treatment —a point not taken into account in the reviewed literature; and c) this is the second Latin American study on the epidemiology of infections in ICUs,[10] and the first of its kind in Colombia —thus allowing us to estimate the behavior of such infections in our country with respect to the situations found elsewhere.

One of the limitations of the study is that the relationship between sample positivity and possible microorganism resistance to the antibiotic used was not known. Likewise, we did not establish the time elapsed from the start of antibiotic treatment to the moment of sample collection; as a result, we are unable to conclude whether or not antibiotic use before sampling affects the positivity data obtained. Likewise, there was no control over whether the different cultures were to be obtained or not —this decision being left to the supervising physician. This determined, for example, that blood cultures were only made in 54.4% of the patients.

It must be remembered that this is a sub-study, and that another article currently in the preparatory phase will detail the microbial resistance profiles in Colombian ICUs and the corresponding multiresistance patterns.

In conclusion, respiratory infections were the infections most commonly found in ICUs in this country. Likewise, *E. coli* was the predominant microorganism in the main out-hospital infections, while in the nosocomial infections *E. coli* shared its importance with *S. aureus* and *K. pneumoniae*.

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Conflict of interest

The authors declare no conflict of interest in the conduction of this study.

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