The epidemiology of sepsis in Colombia: A prospective multicenter cohort study in ten university hospitals*

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Objective: **Our aim was to determine the frequency and the clinical and epidemiologic characteristics of sepsis in a hospital-based population in Colombia.**

Design: **Prospective cohort.**

Setting: **Ten general hospitals in the four main cities of Colombia.**

Patients: **Consecutive patients admitted in emergency rooms, intensive care units, and general wards from September 1, 2007, to February 29, 2008, with confirmation of infection according to the Centers for Disease Control and Prevention definitions.**

Interventions: **None.**

Measurements and Main Results: **The following information was recorded: demographic, clinical, and microbiologic characteristics; Acute Physiology and Chronic Health Evaluation II and Sequential Organ Failure Assessment scores; requirement for intensive care unit; length of stay; and 28-day all-cause mortality. During a period of 6 months, 2,681 patients were recruited: 69% and 31% with community-acquired and hospital-acquired infections, respectively. The mean age was 55 yrs (SD = 21), 51% were female, and the median length of stay was 10 days (interquartile range, 5–19). The mean Acute Physiology and Chronic Health Evaluation score was 11.5 (SD = 7) and the mean Sequential Organ Failure Assessment score was 3.8 (SD = 3). A total of 422 patients with community-acquired infections (16%) were admitted to the intensive care unit as a consequence of their infection and the median length of stay was 4.5 days in the intensive care unit. At admission, 2516 patients (94%) met at least one sepsis criterion and 1,658 (62%) met at least one criterion for severe sepsis. Overall, the 28-day mortality rates of patients with infection without sepsis, sepsis without organ dysfunction, severe sepsis without shock, and septic shock were 3%, 7.3%, 21.9%, and 45.6%, respectively. In community-acquired infections, the most frequent diagnosis was urinary tract infection in 28.6% followed by pneumonia in 22.8% and soft tissue infections in 21.8%. Within hospital-acquired infections, pneumonia was the most frequent diagnosis in 26.6% followed by urinary tract infection in 20.4% and soft tissue infections in 17.4%.**

Conclusions: **In a general inpatient population of Colombia, the rates of severe sepsis and septic shock are higher than those reported in the literature. The observed mortality is higher than the predicted by the Acute Physiology and Chronic Health Evaluation II score. (Crit Care Med 2011; 39:1675–1682)**

KEY WORDS: sepsis; severe sepsis; septic shock; sepsis epidemiology; Colombia; prospective cohort

Sepsis remains a significant and underestimated health problem (1–4). From large epidemiologic studies, sepsis emerges as a common disorder and its frequency and mortality rate exceed the number of other diseases that hold a heightened public awareness such as AIDS and breast cancer (5). In settings other than intensive care units (ICUs), sepsis is also a relatively common reason for acute care hospitalization occurring in 700,000 people each year in the United States and being responsible for 2% of all hospitalizations (6, 7). Care of patients with sepsis has an economic impact for the society that is beyond the one caused by other acute diseases, an economic burden of nearly $17 billion annually in the United States alone (7) with $50,000 per patient only in ICU (8). However, the impact in developing countries is partially known because we are lacking reliable and complete information about this problem. In a recent systematic review, we found that the clinical and epidemiologic approaches to sepsis in Latin America have been apparently inappropriate with respect to research design, study population, and clinical outcomes. Nevertheless, some data suggest that in terms of both frequency and mortality, the situation with sepsis and severe bacterial infections

***See also p. 1833.**

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Dr. Jaimes conceived, designed, and directed this study. All authors supervised the study in each hospital: Drs. Rodríguez and Jaimes in Hospital San Vicente de Paúl; Dr. Barrera in Hospital Universitario del Valle; Dr. De La Rosa in Hospital Pablo Tobón Uribe; Dr. Dennis in Fundación CardioInfantl; Dr. Dueñas in Hospital Bocagrande and Clínica Madre Bernarda; Dr. Granados in Fundación Valle del Lili; Dr. Londoño in Hospital San Ignacio; Dr. Molina in Clínica Universitaria Bolivariana; and Dr. Ortiz in Hospital Santa Clara. Drs. Rodríguez and Jaimes wrote the first draft of the article and all coauthors commented on the draft. All authors provided comments and approved the final article.

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may be worse in Latin America compared with developed countries (9).

To characterize the epidemiology of sepsis in a developing country, we performed a prospective multicenter study to determine the frequency, clinical and epidemiologic characteristics, and the outcomes of sepsis and acute bacterial infections in an inpatient population in Colombia.

METHODS

Settings and Study Design. This was a prospective multicenter cohort study with patients admitted to ten hospitals in the four main cities of Colombia from September 1, 2007, to February 29, 2008. We Included patients from emergency rooms, ICUs, and hospital wards covering both community- and hospital-acquired infections. Patients were considered eligible if they were >18 yrs; had a probable or confirmed diagnosis of infection according to medical records; or had changes in temperature (>38 or <36°C) or hypotension without a specific cause. Furthermore, as definitive inclusion criterion, patients must have had an infection that fulfilled standard Centers for Disease Control and Prevention definitions (10). Patients were excluded if they refused to participate, were screened for eligibility >24 hrs after suspicion of infection, stayed >48 hrs in another institution immediately before the current hospitalization, were not available for 28-day follow-up, were discharged <24 hrs after hospitalization, their diagnosis changed toward a noninfectious disease during hospitalization, or were previously recruited in the study. Hospital-acquired infections were defined as those not present or incubating at the time of admission to the hospital, i.e., infections that become evident ≥48 hrs after admission. The study protocol was approved by the institutional review board at each center. Oral informed consent was obtained in all hospitals except in two in which written informed consent was requested.

Institutions. Ten general and university hospitals in four cities with the largest population in Colombia were invited to participate on the basis of their geographic relevance in every place. These hospitals were sampled by convenience because they are among the biggest institutions in each city and also they are the centers of clinical practice for the investigators. The hospitals were Fundación Cardio-Infantil, Hospital Universitario San Ignacio, and Hospital Santa Clara in Bogotá; Fundación Valle del Lili and Hospital Universitario del Valle in Cali; Clínica Madre Bernarda and Hospital de Bocagrande in Cartagena; and Hospital Pablo Tobón Uribe, Clínica Universitaria Bolivariana, and Hospital Universitario San Vicente de Paúl in Medellin. The latter hospital also served as the coordinating center jointly with the Department of Internal Medicine–University of Antioquia. Only two hospitals (Hospital Santa Clara and Hospital Universitario del Valle) are public institutions.

Data Collection, Evaluation, and Quality Control. There were one or two trained nurses, according to the number of beds, in each hospital. They followed a study protocol standardized twice in 2-day workshops developed within a 3-month pilot study, which was conducted immediately before starting the recruitment. In each hospital, there was also a clinician coinvestigator who was in charge of checking data accuracy and consistency as well as the patient's diagnosis. In addition, the case report forms were checked and revised weekly in a double-entry form in the Data Coordinating Center (Universidad de Antioquia). Any inconsistency, inaccuracy, or missing data implied returning the specific case report form to the coinvestigator for correction within the next week after the Data Coordinating Center review. There was also onsite evaluation during the first month of the study at each hospital by one of the coprincipal investigators. At the recruiting areas of the hospitals, all the inpatients were actively screened for the presence of infection. The severity of illness was assessed using the Acute Physiologic and Chronic Health Evaluation II score (11), and the frequency and magnitude of organ dysfunction was measured with the Sequential Organ Failure Assessment score (12), both determined within the first 24 hrs after enrollment of the patient. We recorded also demographic characteristics, first admission diagnosis and comorbidities, clinical status as sepsis, severe sepsis or septic shock (see definitions in appendix, modified from http://www.ihi.org/IHI/Topics/CriticalCare/Sepsis/Tools/SepsisDefinitions.htm, accessed April 4, 2010), any microbiological report and antibiogram during the first 7 days after enrollment, ICU admission, and vital status at hospital discharge. All patients, regardless of specialties, were visited daily during their hospital stay to determine his or her outcome. For patients discharged before 28 days, their vital status was confirmed by telephone call or outpatient control.

Study Outcomes. The outcomes were 28-day mortality rate, hospital length of stay, ICU admission, frequency of sepsis, and development of severe sepsis and septic shock during the first 24 hrs of hospitalization.

Statistical Analysis. Results are expressed as mean ± SD, median and interquartile range, or proportions according to the type and distribution of the variable. There was not a formal calculation of sample size given the expected variability in the frequency of sepsis and severe sepsis within and among hospitals. However, we estimated a minimum of 6,000 screened participants to obtain a cohort of at least 1,500 patients. This sample size would be able to detect an incidence at least of 4 ± 1 cases of sepsis per 100 hospital admissions and also a wide range of proportions and precisions for severe sepsis, septic shock, and mortality (e.g., 10 ± 1.5%; 20 ± 2%; 40 ± 2.5%, and 50 ± 3%; Epi-Info 3.3, CDC, Atlanta, GA). Data were analyzed by community-acquired or hospital-acquired infection status and for public vs. private institutions. Continuous variables were compared with Student's t test and dichotomous variables with chi square. For all the comparisons, a p value <.05 was considered statistically significant. The database was recorded in Access (Microsoft Office; Microsoft Inc, Redmond, WA) and all the statistical analyses were performed with

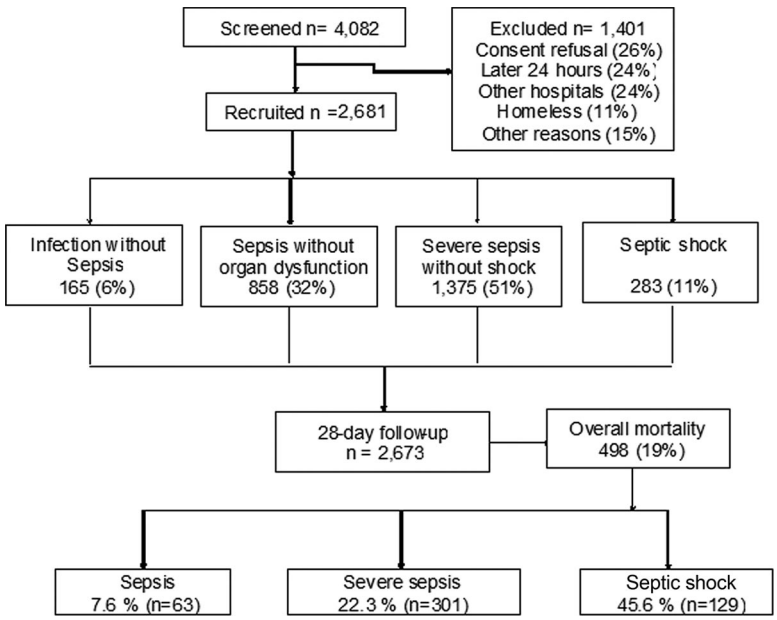

Figure 1. Study population.

Table 1. Characteristics of patients at admission

	Community (69%, n = 1846)	Hospital (31%, n = 835)
City		
Bogota	547 (29.6)	218 (26.1)
Medellin	660 (35.7)	202 (24.2)
Cali	408 (22.1)	378 (45.3)
Cartagena	231 (12.5)	37 (4.4)
Age, yrs	55.8–20.7	53.7–20.2
Males	881 (47.7)	435 (52.1)
Race		
Latin American	1663 (90.1)	722 (86.5)
Afro Colombian	114 (6.2)	68 (8.1)
Others	69 (3.7)	45 (5.4)
Comorbidities		
None	722 (39.1)	157 (18.8)
Trauma or surgery	320 (17.3)	444 (53.2)
Diabetes mellitus	297 (16.1)	111 (13.3)
Chronic renal disease	186 (10.1)	95 (11.4)
Heart failure	161 (8.7)	105 (12.6)
Chronic obstructive pulmonary disease	190 (10.3)	75 (9.0)
Cancer	162 (8.8)	56 (6.7)
Corticosteroid use	134 (7.2)	44 (5,3)
HIV/AIDS	69 (3.7)	25 (3.0)
Alcoholism	63 (3.4)	26 (3.1)
Transplantation	38 (2.0)	14 (1.7)
Chronic hepatic disease	24 (1.3)	12 (1.4)
Acute Physiology and Chronic Health Evaluation II	11.6–7.0	11.6–6.6
Sequential Organ Failure Assessment	3.6–3.1	4.1–3.2

Data are presented as no. (%) or mean–SD.

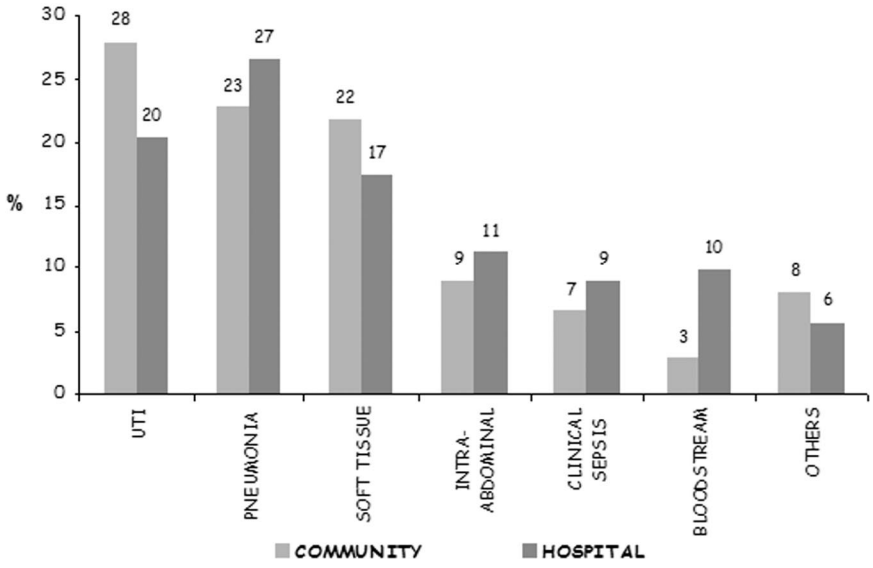

Figure 2. Sources of infection. *UTI*, urinary tract infection.

STATA (release 10; Stata Corp, College Station, TX).

RESULTS

Between September 1, 2007, and February 29, 2008, a total of 49,739 patients were admitted by the emergency rooms of the institutions. Among them, 4,082 were considered eligible to participate and 1,401 were excluded, mainly because of consent refusal (26%), screening for eligibility >24 hrs after suspicion of infection (24%), and stay >48 hrs in another institution immediately before the current hospitalization (24%), among other causes (Fig. 1). Finally, 2,681 patients were recruited and included in the analysis: 1,846 (69%) with community-acquired infections and 835 (31%) with hospital-acquired infections. The mean monthly admission by emergency room was 866 patients per institution, and the mean number of occupied adult beds monthly per institution was 240. Accordingly, and assuming a constant occurrence of infection, the monthly cumulative incidence rate of sepsis was 3.61 per 100 admissions per hospital and the monthly period prevalence was 18.6% per hospital. At recruitment, 2,516 patients (94%) met at least one sepsis criterion and 1658 (62%) met at least one criterion for severe sepsis (Fig. 1). The mean age was 55 yrs (SD = 21 yrs), 1,365 (51%) were female, the mean Acute Physiologic and Chronic Health Evaluation II score was 11.5 (SD = 7), and the mean Sequential Organ Failure Assessment score 3.8 (SD = 3). The most common comorbidities were trauma or surgery in 28.5% (n = 764), diabetes mellitus in 15.2% (n = 408), chronic renal disease in 10.5% (n = 281), heart failure in 9.9% (n = 266), and chronic obstructive pulmonary disease in 9.9% (n = 265). Among the total cohort, 879 patients (33%) did not have any comorbidity. The characteristics of the study population at admission, classified by site of acquisition of infection, are shown in Table 1.

Patterns of Infections and Microbiology. In community-acquired infections, the most frequent diagnosis was urinary tract infection (527 patients [28.6%]) followed by pneumonia (421 patients [22.8%]) and soft tissue infections (402 patients [21.8%]). In hospital-acquired infections, instead, pneumonia was the most frequent diagnosis (222 patients [26.6%]) followed by urinary tract infection (170 patients [20.4%]) and soft tissue infections (145 patients [17.4%]) (Fig. 2). At least one microbiologic sample was obtained for culture from 1761 participants (66%) and blood cultures were the most requested sample obtained from 1045 (39%) with 375 of these (36%) yielding a positive result. Gram-negative bacteria were the most frequent pathogens in blood cultures (n = 216 [58%]), and Gram-positive microorganisms were recovered from 40% (n = 150) of the samples. Fungus represented 2% (n = 8) of the positive blood cultures. Overall, the most common bacteria were *Escherichia coli* in 22.9% followed by *Staphylococcus au-*

Table 2. Infections and results of blood cultures

Community-Acquired Infections (N = 1846)			Hospital-Acquired Infections (N = 835)		
	Blood Cultures			Blood Cultures	
Infection	Requested[a]	Isolated[b]	Infection	Requested[a]	Isolated[b]
Urinary tract infection 449 (24.3%)	173 (66, 38%)	*Escherichia coli* (36) *Klebsiella pneumoniae* (6) *Staphylococcus aureus* (4) CNS (4) *M. morganii* (2) *Pseudomonas aeruginosa* (2) *Staphylococcus epidermidis* (2) Others (10)	Urinary tract infection 122 (14.6%)	27 (11, 41%)	*S. aureus* (3) *E. coli* (2) *Staphylococcus haemolyticus* (2) Others (4)
Pneumonia 417 (22.6%)	175 (35, 20%)	*Escherichia coli* (5) *K. pneumoniae* (5) *Streptococcus pneumoniae* (5) CNS (4) *S. aureus* (4) *S. epidermidis* (3) Others (9)	Nosocomial pneumonia 221 (26.5%)	81 (30, 37%)	*S. epidermidis* (6) *E. coli* (4) *Acinetobacter baumannii* (3) *K. pneumoniae* (3) *S. aureus* (3) CNS (2) *Enterobacter cloacae* (2) Others (7)
Soft tissue infections 332 (18%)	96 (28, 29%)	*S. aureus* (12) *E. coli (4)* *Morganella morganii* (2) CNS (2) Others (8)	Soft tissue infections 55 (6.6%)	15 (9, 60%)	*K. pneumoniae* (3) *P. aeruginosa* (2) Others (4)
Intra-abdominal 164 (8.9%)	71 (23, 32%)	*E. coli* (7) *K. pneumonia* (4) *S. epidermidis* (3) Others (9)	Intra-abdominal 93 (11.1%)	36 (12, 33%)	*E. coli* (4) *P. aeruginosa* (2) *S. pneumoniae* (2) Others (4)
Primary bacteremia 43 (2.3%)	43 (43, 100%)	*E. coli* (8) *K. pneumoniae* (8) *S. aureus* (6) *P. aeruginosa* (5) *Candida albicans* (2) *Enterococcus faecalis* (2) Others (12)	Primary bacteremia 51 (6.1%)	51 (51, 100%)	*K. pneumoniae* (12) *S. aureus* (9) *A. baumannii* (4) *E. cloacae* (4) *S. epidermidis* (3) *E. coli* (3) *P. mirabilis (2)* *K. oxytoca (2)* Others (12)
Gastroenteritis 53 (2.9%)	19 (2, 11%)	*E. coli* (1) *K. pneumonia* (1)	Surgical site infections 52 (6.2%)	7 (1, 14%)	*K. pneumoniae* (1)
Others 388 (21%)	144 (33, 23%)	*E. coli* (7) *S. aureus* (6) *K. pneumonia* (2) *Streptococcus viridans* (2) *Streptococcus milleri* (2) *Klebsiella oxytoca* (2) Others (12)	Others 241 (28.9%)	107 (39, 36%)	*S. aureus* (8) *Candida albicans* (4) *E. coli* (4) *Serratia marcescens* (4) *P. aeruginosa* (3) *K. pneumoniae* (2) Others (14)

CNS, coagulase-negative staphylococci; Others, any of *Achromobacter xylosoxidans, Bacillus cereus, Bacillus* spp, *Campylobacter jeikeium, Candida glabrata, Cedecea lapagei, Citrobacter koseri, Corynebacterium* spp, *Enterobacter sakazakii, Enterococcus* spp, *Listeria monocytogenes, Listeria* spp, *Providencia rettgeri, Providencia rustigianii, Pseudomonas fluorescens, Pseudomonas putrida, Salmonella typhi, Salmonella* spp, *Staphylococcus auricularis, Staphylococcus capitis, Staphylococcus saprophyticus, Streptococcus gordonii, Streptococcus pyogenes*, other Gram-negative bacteria, or other unclassified micro-organisms.

[a]Between parentheses are the absolute numbers and the percentage of positive blood cultures; [b]between parentheses are the numbers of isolates of this micro-organism in each type of infection.

reus in 15.7% and *Klebsiella pneumoniae* in 13.1% (Table 2).

Outcomes. Among 2673 patients followed for 28 days, there were 498 deaths (18.6%). Overall, 28-day mortality rates for patients with infection without sepsis, sepsis without organ dysfunction, severe sepsis without shock, and septic shock were 3% (n = 5), 7.6% (n = 63), 22.3% (n = 301), and 45.6% (n = 129), respectively. Although the proportion of severe sepsis and septic shock was similar as well as the mean Acute Physiologic and Chronic Health Evaluation II score in community- and hospital-acquired infections, 28-day mortality rate and length of stay were higher in the later (Table 3). Among the population with community-acquired infections, 422 (22.9%) required ICU attention. Furthermore, among the 835 patients with hospital-acquired infections, 360 (43.1%) had specifically an ICU-acquired infection. The only two public hospitals accounted for 37.3% (n = 1001) of the total study population. There were statistically significant differences in age (p = .000), Sequential Organ Failure Assessment score (p = .000), and 28-day mortality (p = .000) between public and private institutions (Table 4).

Table 3. Outcome measures[a]

	Community (n = 1846)	Hospital (n = 835)
28-day mortality	303 (16.4%)	195 (23.4%)
Length of stay for survivors	8 (4–14)	20 (11–33)
Length of stay for nonsurvivors	5 (3–10)	12 (7–22)
Sepsis	615 (33.3%)	243 (29.1%)
28-day mortality	34 (5.5%)	29 (12.0)
Length of stay for survivors	6 (3–10)	16 (8–27)
Length of stay for nonsurvivors	7 (5–14)	20 (8–25)
Severe sepsis	928 (50.3%)	447 (53.5%)
28-day mortality	189 (20.5%)	112 (25.1%)
Length of stay for survivors	9 (6–15)	22 (13–35)
Length of stay for nonsurvivors	4 (3–9)	12 (8–22)
Septic shock	184 (10.0%)	99 (11.9%)
28-day mortality	77 (42%)	52 (52%)
Length of stay for survivors	13 (9–20)	28 (17–44)
Length of stay for nonsurvivors	5 (3–11)	10 (6–18)

[a]Data are presented as number and percentages or median and interquartile range.

Table 4. Main characteristics of study population in public and private hospitals[a]

	Public (n = 1001)	Private (n = 1680)	*p*
Age	52.6–20.4	56.6–20.5	.000
Male	515 (51.4)	801 (47.7)	.059
Acute Physiology and Chronic Health Evaluation	11.8–7.2	11.5–6.6	.220
Sequential Organ Failure Assessment	4.1–3.5	3.6–2.9	.000
Severe sepsis	536 (53.5)	839 (50)	.071
Septic shock	115 (11.5)	168 (10)	.225
28-day mortality	230 (23)	268 (16)	.000
Intensive care unit attention	315 (31.5)	511 (30.5)	.596

[a]Data are presented as no (%) or mean–SD.

DISCUSSION

Our study showed some interesting findings regarding sepsis in Colombia. It affects a comparatively young (mean age, 55 yrs) and healthy (33% of the cohort without previous comorbidity) population. The occurrence of hospital-treated infections in general, and the frequencies of severe sepsis (51%) and septic shock (11%) in particular, are much higher than those expected in a general unselected impatient population. Although the mortality rates of patients who met criteria for severe sepsis and septic shock (22% and 46%, respectively) are similar to those reported in other studies (7, 13), the overall 28-day mortality rate of 19% is higher than the expected according to a mean Acute Physiologic and Chronic Health Evaluation II score of 11.5 (i.e., 14%). Finally, contrary to the common finding in developed countries (6, 14–16), Gram-negative bacteria are responsible for the majority of positive blood cultures compared with Gram-positive micro-organisms (58% vs. 40%).

Several studies from different countries have reported a high estimated incidence of sepsis in the general population, and this condition appears to be increasing over the last years (6, 13, 15, 17–19). However, most of these studies were conducted only at ICUs or using databases of administrative healthcare information. Furthermore, the majority of representative epidemiologic reports of sepsis is also from developed countries; thereby, it is difficult to compare their results with our findings and even the results among those studies. Our study is the first one that has prospectively studied the current status of sepsis in adult patients hospitalized in institutions of the highest level within the Colombian health system. As a remarkable issue, we have included not only patients with severe sepsis and septic shock, but also patients without evidence of organ dysfunction. Although we could not determine exactly a nationwide estimate of incidence or prevalence, our data do show that sepsis is a significant burden of illness and death in our community. Compared with the most recent studies, our cohort represents the largest prospectively collected with the widest clinical range within any hospital-based population with acute bacterial infections and sepsis (Table 5). There is only one similar study that was conducted >15 years ago by Rangel-Frausto et al (29) in Iowa and its results were overly different. They assessed the incidence of systemic inflammatory response syndrome, sepsis, severe sepsis and septic shock among 3708 patients admitted during a 9-month period to three ICUs and three general wards in a unique tertiary healthcare institution. During the study period, 3708 patients were admitted to the survey units, and 2527 (68%) met the criteria for systemic inflammatory response syndrome. Among patients with systemic inflammatory response syndrome, 649 (26%) developed sepsis, 467 (18%) severe sepsis, and 110 (4%) septic shock. Positive blood cultures were found in 16.5%, 25.4%, and 69% of the samples drawn from patients with sepsis, severe sepsis, and septic shock, respectively (29).

Given the high sensitivity of the sepsis criteria considered in our research, the vast majority of patients met at least the definition of sepsis and just 6% were recruited with acute bacterial infections but without markers of systemic response (i.e., without findings indicative of sepsis). This wide definition may explain the relatively high frequency of septic patients. However, the physical signs and laboratory findings used to define organ dysfunction and septic shock are standard criteria as well as the formal Centers for Disease Control and Prevention definitions of infection (10, 30). Therefore, severe sepsis in our cohort is not overestimated but more precisely defined and misclassification is an extremely unlikely explanation for our findings.

The younger affected population, their relatively high mortality rate, and the kind of micro-organisms identified with predominantly Gram-negative bacteria suggest that sepsis epidemiology in our country is 25 yrs behind the current epidemiology of sepsis in the United States and other developed nations. The study by Martin et al (6) studied the epidemiology of sepsis in United States from 1979 through 2000 according to data drawn

Table 5. Recent epidemiologic studies on sepsis

Country	Design and Time	Patients	Age, yrs (Median)	Mortality		
				Sepsis	Severe Sepsis	Septic Shock
Thailand (20)	Prospective one center, 2 yrs	390 new admissions aged >15 yrs with severe sepsis or septic shock	56	ND	21.8% in ICU; 34.5% in hospital	44.2% in ICU; 54.1% in hospital
Thailand (21)	Prospective one center, 6 months	201 sepsis patients in medical wards	ND	34.3%	ND	52.6%
Spain (18)	Prospective multicenter cohort, 6 months	324 episodes of severe sepsis among 311 patients >18 yrs in 14 ICUs	68	ND	54.3% in hospital, 47.9% at 28 days, 52.4% at 60 days, and 53.7% at 90 days	ND
Brazil (22)	Prospective one center, 6 months	342 patients >18 yrs with severe sepsis/septic shock among 5332 admitted to the emergency department	73.7	ND	64%	
Chile (23)	Prospective multicenter cross-sectional, 1 day	289 patients >16 yrs in 60 ICUs, 112 with severe sepsis	57.9	ND	25.9% at 28 days	ND
Spain (13)	Prospective multicenter cohort, 4 months	702 sepsis patients among 15852 adults admitted in three hospitals	69	6.7% in hospital	20.7% in hospital	45.7% in hospital
Germany (14)	Prospective multicenter cross-sectional, 1 day	1348 infected patients among 3877 ICU admissions of 310 hospitals	68	ND	55.2% in hospital	ND
Finland (24)	Prospective multicenter cohort, 4 months	470 patients with severe sepsis among 4500 ICU admissions >18 yrs old in 24 ICU	59.6	ND	15.5% in ICU, 28.3% in hospital, 40.9% at 1 yr	ND
24 European countries (15)	Prospective multicenter observational, 2 independent days	3,147 adult >15 yrs in 198 ICUs, 1177 (37.4%) had sepsis, 30% severe sepsis, and 15% septic shock	64	27% in ICU	32.2% in ICU	54.1% in ICU
Brazil (25)	Prospective multicenter cohort, 10 months	1383 adult in five ICUs	65.2	34.7% at 28 days	47.3% at 28 days	52.2% at 28 days
France (16)	Prospective multicenter survey, 2 wks	Among 3738 admissions to 206 ICUs, 14.6% patients experienced severe sepsis/septic shock	65	ND	35% at 30 days, 41.9% at 2 months	
Slovenian (26)	Retrospective multicenter survey, 2 wks	91 patients with severe sepsis among 701 admissions to 28 ICUs	76.1	ND	45.1% at 28 days	ND
Turkey (27)	Retrospective search of hospital charts, 2 months	69 episodes with diagnostic code of sepsis/septicemia/ bacteremia	61.8	76.8% at 28 days	92.2% at 28 days	ND
Taiwan (28)	Nationwide population-based database, 10 yrs	5258 patients with severe sepsis hospitalized in Taiwan between January 1, 1996, and December 31, 2006	69.5 (1997–1998), 70 (1999–2000), 71 (2001–2002), 73 (2003–2004), 74 (2005–2006)	ND	The hospital mortality rate averaged 30.8% and changed little during the study period	ND

ICU, intensive care unit; ND, no data.

from the National Hospital Discharge Survey database. They found a mean age of 60.8 yrs for the period between 1995 and 2000 compared with 57.4 yrs for the initial period (1979–1984). They also showed that from 1979 through 1987, Gram-negative bacteria were the predominant organisms causing sepsis, whereas Gram-positive bacteria were reported most commonly in each subsequent year. Among the organisms reported to have caused sepsis in 2000, Gram-positive bacteria accounted for 52.1% of cases with Gram-negative bacteria accounting for 37.6% and fungi for 4.6%. Recently, the study by Esteban et al (13) was a prospective observational study with ICU and non-ICU patients from three academic hospitals in Madrid, Spain. Sepsis was identified in 702 patients during 4 months with an estimated cumulative incidence rate of 367 cases per 100,000 adult area residents per year and a cumulative incidence among patients admitted to the hospital of 4.4%. The mean age was 69 yrs and the hospital mortality for all septic patients was 12.8%; for severe sepsis, it was 20.7% and for septic shock, it was 45.7% (13). Although their mortality rates resemble closely our findings, the

mean age was considerably higher for a similarly unselected population. On the other hand, a study in China in ten ICUs of university hospitals found some results potentially comparable to our "developing" findings (31); although the median age of patients with severe sepsis was 64 yrs, 53.8% of isolates were Gram-negative and 45.9% were Gram-positive bacteria. Similarly, the overall hospital mortality was 48.7% despite a median Acute Physiologic and Chronic Health Evaluation II of 19, suggesting an expected mortality considerably lower than the observed. We have not a clear explanation for our comparatively higher rates of severe sepsis, septic shock, and mortality. However, it is interesting to speculate about three potential reasons: 1) genetic and/or physiological differences in our study population (32); 2) local difficulties in the recognition of sepsis, because our services and practitioners may lack the required diagnostic capability for sepsis; and 3) late referral to ICUs, because the shortage of critical care beds and the late recognition of severe sepsis could delay admission to the ICU. Furthermore, the relatively high rate of exclusions (34% of the eligible population) deserves special attention. More than 50% of them would be true sepsis cases in our cohort, because the reasons for their exclusion were not related to the disease: refusal to participate (26%), detection by the research assistants >24 hrs after infection diagnosis (24%), and homeless (11%). This situation suggests that our results might underestimate the incidence of sepsis, and the magnitude of the problem could be even worse in our country.

Finally, two of ten institutions in our study were public hospitals, and their patients accounted for more than one-third of the total cohort. Additionally, the overall 28-day mortality was higher for public (23%) than for private (16%) institutions. This difference in mortality was also found in the study by Silva et al in Brazil (25), that noted that public hospitals attended younger patients but with higher Sequential Organ Failure Assessment scores, similar findings to those of our study. In Chile, on the other hand, there were no differences in Sequential Organ Failure Assessment score or mortality between patients from 33 public and 27 private ICUs (23). Although some differences in the treatment and in achieving early goals may exist between public and private hospitals, we cannot answer this question given the observational condition of the current study. Therefore, further trials to specifically evaluate this issue are warranted.

CONCLUSIONS

In this prospective multicenter study of ten referral hospitals in Colombia, we found that the frequency of severe sepsis and septic shock are much beyond the figures reported throughout the world. These findings should be evaluated carefully according to the age of the affected population, their previous health status, their microbiologic characteristics, and the relatively unexpected mortality. This suggests that a priority for our national health system, and probably for the majority of developing countries, should be to define strategies for prevention and a better control of this problem and its burden of morbidity and mortality.

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Appendix 1. Clinical definitions[a]

Sepsis
- Infection that fulfilled standard Centers for Disease Control and Prevention definitions and one of the following:
  - A. Fever (core temperature >38.3°C) or hypothermia (core temperature <36°C)
  - B. Altered mental status (Glasgow Coma Scale <15)
  - C. Heart rate >90 beats/min
  - D. Respiratory rate >20 breaths/min
  - E. Significant edema or positive fluid balance (>20 mL/kg over 24 hrs)
  - F. Plasma glucose >120 mg/dL (7.7 mmol/L) in the absence of diabetes
  - G. White blood cell >12,000 cells/μL (or >15,000 cells/μL in postpartum women)
  - H. Plasma C-reactive protein >5 mg/dL

Severe sepsis
- Severe sepsis is defined in the presence of the least one variable of organ dysfunction, hypoperfusion, or hypotension
- Organ dysfunction
  - A. Arterial hypoxemia (PaO_2/FIO_2 <300)
  - B. Acute oliguria (urine output <0.5 mL/kg/hr for at least 2 hrs)
  - C. Serum creatinine >2 mg/dL
  - D. Coagulation abnormalities (international normalized ratio >1.5 or activated partial thromboplastin time >60 secs)
  - E. Platelet count <100,000 cells/μL
  - F. Plasma total bilirubin >2 mg/dL
- Hypoperfusion
  - A. Serum lactate >2 mmol/L
  - B. Decreased capillary refill >2 secs
  - C. Unexplained metabolic acidosis (arterial pH <7.3)
- Hypotension
  - A. Systolic blood pressure <90 mm Hg or a decrease >40 mm Hg with respect to previous values or mean arterial blood pressure <60 mm Hg

Septic shock
- State of acute circulatory failure characterized by persistent arterial hypotension (as defined previously) despite adequate volume resuscitation or need of vasoactive drugs by continuous infusion over 6 hrs regardless of the values found in the initial measure of blood pressure.

Modified from http://www.ihi.org/IHI/Topics/CriticalCare/Sepsis/Tools/SepsisDefinitions.htm. Accessed April 4, 2010.