ORIGINAL ARTICLE

Epidemiology of infections treated in hospital emergency departments and changes since 12 years earlier: the INFURG study of the Spanish Society of Emergency Medicine (SEMES)

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Objectives: To estimate the prevalence of infectious disease treated in Spanish hospital emergency departments and to describe the characteristics and management of patients with infections and their clinical course in comparison with a cohort studied 12 years earlier.

Methods: Multicenter descriptive, cross-sectional study of 49 Spanish emergency departments on the 10th and 20th day of each of 12 months. To estimate prevalence we registered cases in which the diagnosis was infection, noting the location of infection and the total number of times the patient was attended during the study period. To describe patient characteristics and management, we recorded demographic data, concomitant diseases, risk factors for multidrug resistant infection, microbiologic tests ordered, antibiotic treatments prescribed, destination on discharge, and mortality before discharge.

Results: The prevalence of infectious diseases in the participating emergency departments was 14.3% (4.6%, respiratory tract; 3.2% urinary tract; 2.1%, ear-nose-throat; 1.6%, skin and soft-tissues; and 2.8% other). Infections related to diabetes mellitus, heart disease, or chronic obstructive pulmonary disease accounted for 4543 (39.8%) of the total, and 707 (6.2%) patients had sepsis on arrival. Microbiology was not ordered in 6463 cases (56.7%), and amoxicillin-clavulanic acid was the most frequently prescribed antibiotic, used in 3600 cases (31.6%). A total of 1022 patients (9%) were already taking antibiotics when they came to the emergency department. Forty-six patients (0.5%) died before discharge from the department and 2653 (23.3%) were hospitalized.

Conclusions: Patients with infections, especially involving the respiratory or urinary tracts, account for a large proportion of the Spanish hospital emergency department caseloads studied. We observed an increase in the prevalence of infection in comparison with the study 12 years earlier. Patients in the recent study were older, were more often septic, and had more concomitant diseases and more risk factors for multidrug resistant infections. [Emergencias 2013;25:368-378]

Keywords: Infections. Epidemiology. Emergency health services. Antibiotics. Mortality. Sepsis. Bacteremia.

Introduction

Infectious diseases are a major health problem in the world. They are associated with high morbidity and mortality in all areas of healthcare, including hospital emergency departments (EDs)[1]. In Spain, for three decades now, numerous studies report that these represent 5-17% of ED patients attended, as well as being one of the leading causes of hospital admission and mortality[2,3]. Infectious diseases have great impact on the need for microbiological studies and antimicrobial treatment, involving human and economic costs.

In the year 2000, the Journal Emergencias published a paper on the study of infection in the ED by the working group of the Spanish society of Emergency Medicine (SHEMESH), describing the prevalence of infections, their characteristics and those of the patients that are diagnosed, management carried out of these patients and the therapeutic used before and after consultationall in the field of the EDs[4]. That study found that infections accounted for 10.4% of all patients attended in the EDs studied, with a prevalence of respiratory infection (3.2%), followed by the urinary infection (2.1%). One in twenty patients with infectious diseases met sepsis criteria on ED arrival, and the percentage of global admission was 20.6% with respiratory infection being the most common reason.

A decade later, the INFURG-SHEMESH group examined whether there had been changes in the epidemiology of patients with infection attended in Spanish EDs, the characteristics of patients or their clinical management. The objective of this study, which used similar methodology, was to determine the prevalence and impact of infection in Spanish EDs, as well as the clinical profile and early management of patients with clinical diagnosis of infection in the ED, and compare the results of both studies.

Method

We performed a descriptive, analytical multicenter study carried out in 49 Spanish EDs (see addendum). We included all patients clinically diagnosed with an infectious process in the ED on the 10th day (from 0 to 12 hours) and 20th day (from 12 hours to 24 hours) of each month for a period of 12 months (from October 2010 to September 2011). Patients cared for in the areas of GYN or Pediatrics (under 14 years) were not included. The methodology used in the study was the same as that carried out in the previous epidemiological study[4]. The current study included 14 fewer hospitals due to logistical problems. For the calculation of the prevalence of infection, the number of patients with clinical diagnosis of infection, as well as its location, and the total number of attendance during the study period were recorded. The study was approved by the clinical trials and research committee of the University Hospital de Basurto.

For each patient diagnosed with an infectious process, we collected demographic variables (age, sex), comorbidity (diabetes mellitus, heart disease, obstructive pulmonary disease chronic - COPD - chronic liver disease, chronic renal failure, infection by HIV, solid neoplasia, hematological neoplasm), multidrug resistance risk factors (immunosuppressive treatment, if a carrier of urinary catheter or central catheter, prior hospitalization in the last 3 months, antibiotic in the last month and long-term institutional or nursing home care)[5-7], type of infection, presence or not of clinical sepsis, severe sepsis or septic shock[8], the antibiotic prescribed in EDs, microbiological studies requested in emergency, patient destination (ED observation area, short stay unit, medical or surgical department, intensive care, hospital discharge), and mortality during ED stay.

Registered infections were: urinary (UI) (acute pyelonephritis, lower tract UI, prostatitis, UI in patients with a urinary catheter), lower respiratory tract (LRTI) (acute bronchitis, infectious exacerbation of COPD, infected bronchiectasis, pneumonia, lung abscess), otorhinolaryngological (or ear, nose and throat – ENT) infections (sore throat, sinusitis, otitis, infection of deep neck spaces), intra-abdominal infection (IAI) (hepatobiliary, appendicitis, diverticulitis, peritonitis infection), gastroenteritis, skin and soft tissue (SSTI) (necrotizing infection, non-necrotizing infection, diabetic foot infection, infection of pressure sores), osteoarticular (arthritis, osteomyelitis, articular prosthesis infection), neurological (meningitis, encephalitis), influenza and miscellaneous (ocular infections, herpes zoster, viral fever without a focus, odontogenic, pericarditis, and others). The variable "flu" was specifically considered because of its expected impact in the H1N1 flu pandemic when data recording was carried out. The diagnostic criteria for influenza were fever 37.8°C and acute onset non-productive cough ($\leq$ 48 h) without alveolar infiltrate on chest x-ray (modified Ebell and Alonso[9]).

Registration of the variables was performed using an electronic data collection sheet. The differ-

ent criteria and parameters were defined previously by the Group on the basis of clinical guidelines and consensus, previously published, and subsequently disseminated to members of each participating ED by the principal investigator of each center.

Absolute and relative frequencies were used to describe the qualitative variables and means and standard deviation for quantitative variables. We used Chi square or Fisher's exact test, as appropriate, for qualitative variables and Student's t test for the analysis of the quantitative variables. Comparisons were made by reasons of prevalence (RP) or mean differences (dif.) respectively, with 95% confidence intervals (CI). P values < 0.05 were considered statistically significant or when the 95%CI of the RP excluded the value of 1 or a value of 0 for the 95%CI of the dif. All analysis was conducted using SPSS 19.0.

Results

During the study period, 79,654 patients were treated at the participating EDs. Of these, 11,399 were clinically diagnosed with an infectious process (14.3%). Depending on the location of infection, prevalence was: 4.6% LRTI, 3.2% UI, 2.1% ENT, 1.6% SSTI, 0.6% IAI, 0.9% gastroenteritis, 0.05% Osteoarticular infection, 0.03% central nervous system (CNS), 0.4% flu and 1.3% miscellaneous (Figure 1).

Regarding LRTIs, the most frequent were acute bronchitis (49.4%), pneumonia (29.4%) and infectious exacerbation of COPD (20%). Among the UI, the most frequent was lower tract infection (71.4%). For ENT infections, the most common was sore throat (59.7%). In the IAI, there was a slight predominance of hepatobiliary infection (43.8%), appendicitis (28.6%) and diverticulitis (22.4%). Non-necrotizing SSTI was most frequently observed in this group (81.4%) (Table 1). Mean age was 53 years (SD 23) and 51.2% were women. LRTI presented higher mean age, 64 (SD 21), with greatest frequency in those aged 70-89 years (43.8%; p < 0.001). By contrast, ENT infection affected significantly younger patients (mean 36 years; p < 0.001).UI appeared most frequently in women (64.6% compared to 35.4%; p < 0.001), while LRTI (54.9% versus 45.1%; p < 0.001) and IAI (58.9% versus 41.1%, p < 0.001) was more frequent in male patients (Table 2).

Regarding comorbidity, heart disease (14.9%), diabetes (13.2%), COPD (11.7%) and tumor

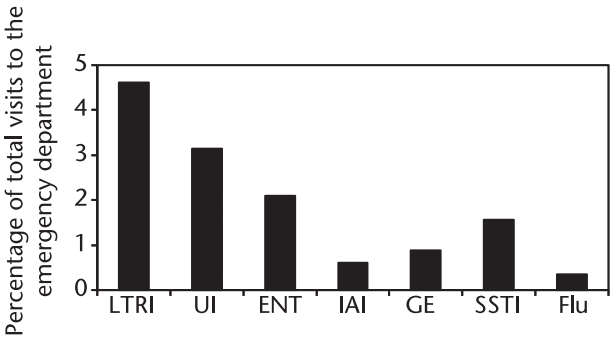

Figure 1. Prevalence of different types of infection. LTRI: Lower Tract Respiratory Infection; UI: Urinary infection; ENT: ear, nose & throat; IAI: intra-abdominal; GE: GastroEnteritis; SSTI: Skin and Soft Tissue Infection. FLU.

Table 1. Type of infection

Type of infection	Total nº (%)
LTRI	3,678 (32.3)
Bronchitis	1,818 (49.4)
Pneumonia	1,083 (29.4)
AECOPD	735 (20)
Bronchiectasis	32 (0.9)
ABSC lung	10 (0.3)
Urinary	2,517 (22.1)
Lower tract	1,798 (71.4)
Pyelonephritis	439 (17.5)
Prostatitis	166 (6.6)
Probe carrier	114 (4.5)
ENT	1,678 (14.7)
Pharyngitis	1,001 (59.7)
Otitis	430 (25.6)
Sinusitis	139 (8.3)
Deep neck spaces	108 (6.4)
SSTI	1,250 (11)
Non-necrotizing	1,017 (81.4)
Necrotizing	147 (11.8)
Diabetic foot	46 (3.6)
PU	40 (3.2)
GE	689 (6)
IAI	482 (4.2)
Hepatobiliary	211 (43.8)
Appendicitis	138 (28.6)
Diverticulitis	108 (22.4)
Peritonitis flu	25 (5.2)
Flu	283 (2.5)
Osteo-articular	41 (0.4)
Arthritis	17 (41.5)
Osteomyelitis	13 (31.7)
Prosthesis infection	11 (26.8)
Neurological	24 (0.2)
Meningitis	13 (54.2)
Encephalitis	11 (45.8)
Miscellaneous	1,009 (8.8)
Eye	279 (27.7)
Odontogenic	244 (24.2)
Fever without focus	180 (17.8)
Viral	150 (14.9)
Herpes zoster	92 (9.1)
Pericarditis	11 (1.1)
Others	53 (5.2)

LTRI: respiratory infections of lower tract; AECOPD: acute exacerbation of chronic obstructive pulmonary disease; ABS: (Lung) abscess; ENT: ear. nose and throat; SSTI: infection of skin and soft tissues; PU: pressure ulcers; AGE: acute gastroenteritis; IAI: intra-abdominal.

Table 2. Age and sex of patients for different types of infection

	Urinary n (%)	LTRI n (%)	ENT n (%)	IAI n (%)	AGE n (%)	SSTI n (%)	Osteoarticular n (%)	NRL n (%)	Flu n (%)	Total n (%)
Mean age (SD)	56 (24)	64 (21)	36* (16)	59 (21)	43 (21)	52 (21)	59 (21)	50 (23)	39 (18)	**53 (23)**
Age group										
14-29 years	491 (19.5)	321 (8.7)	683 (40.7)	55 (11.4)	230 (33.4)	219 (17.5)	4 (9.8)	6 (25)	105 (37.1)	**2,283 (20)**
30-49 years	584 (23.2)	660 (17.9)	699 (41.7)	105 (21.8)	230 (33.4)	392 (31.4)	13 (31.7)	7 (29.2)	108 (38.2)	**3,092 (27.1)**
50-69 years	535 (21.3)	848 (23.1)	203 (12.1)	140 (29)	110 (16)	320 (25.6)	8 (19.5)	4 (16.7)	46 (16.3)	**2,415 (21.2)**
70-89 years	779 (30.9)	1,612 (43.8)*	92 (5.5)	167 (34.6)	112 (16.3)	291 (23.3)	14 (34.1)	7 (29.2)	24 (8.5)	**3,202 (28.1)**
> 90 years	128 (5.1)	237 (6.4)	1 (0.1)	15 (3.1)	7 (1)	28 (2.2)	2 (4.9)	0 (0)	0 (0)	**407 (3.6)**
Sex										
Male	891 (35.4)	2,021 (50.9)*	813 (48.5)	284 (58.9)*	295 (42.8)	703 (56.2)	18 (43.9)	14 (58.3)	134 (47.3)	**5,563 (48.8)**
Female	1,626 (64.6)*	1,657 (45.1)	865 (51.5)	198 (41.1)	394 (57.2)	547 (43.8)	23 (56.1)	10 (41.7)	149 (52.7)	**5,836 (51.2)**

SD: standard deviation; LTRI: respiratory infections of lower tract; ENT: ear, nose and throat; IAI: intra-abdominal infection; AGE: acute gastroenteritis, SSTI: skin and soft tissue infection; NRL: neurological; *p < 0,05.

pathology (9.3%) predominated. Of all comorbidity factors studied (Table 3), diabetes mellitus was significantly associated with the UI and COPD with LRTI (p < 0.001 for both).

Regarding multi-resistant microorganism risk factors, 9% of the patients had taken an antibiotic treatment before their assessment in the ED, 4.3% came from care institutions, immunosuppressive treatment 4.6%, and 3.8% presented a recent admission to hospital (Table 4).

Regarding the severity of clinical presentation, 707 (6.2%) met the clinical criteria for sepsis at the time of ED assessment, 140 (1.2%) severe and 75 (0.7%) septic shock (Table 5). Infections most commonly associated with the presence of sepsis were neurological (16.7% vs. 7.4%; p = 0.009) and IAI (15.4% vs. 7.6%, p < 0.001) (Table 5).

With respect to etiologic documentation of the infectious process, no microbiological evidence was obtained for more than half of the patients (56.7%). When available, it was mainly based on blood (14.6%) and urine cultures (14.6%).

The antibiotics prescribed in the EDs are described in Table 6. Globally the main types used were beta-lactams (45.5%) and of these, amoxicillin-clavulanic acid (31.6%) was most frequently used, followed by fluoroquinolones (23.2%). 18.5% of patients had no record of antibiotic treatment in EDs, mostly for processes of expected viral etiology or they received antibiotic treatment elsewhere after ED admission (operating room, ward or intensive care unit).

Amoxicillin-clavulanic acid was the most commonly used antibiotic in UI (26.5%), ENT (60.8%) and SSTI (60.9%). For LRTI, the most commonly used antibiotics were fluoroquinolones (43.7%) and for IAI piperacillin/tazobactam (19.7%), although there were large differences with respect to carbapenem (18.9%) or amoxicillin-clavulanic acid (18.7%). Antibiotics commonly used in patients meeting sepsis criteria were the fluoroquinolones (29.8%), followed by cephalosporins (26.4%) and amoxicillin-clavulanic acid (19%).

Regarding patient destination, direct discharge from the EDs accounted for 67.4% of infected patients, although this analysis is highly variable depending on the model of infection. Of hospital admissions, medical wards received most patients (20%), followed by observation units (7.1%), surgical departments (2.8%) and short stay units (1.8%) (Table 5).

A total of 46 (0.4%) patients died of infection during ED stay. Mean age was 78 years (SD 15) and 41 (89.1%) were older than 70 years. The infectious process responsible for the death in 30 cases (65.3%) was LRTI, 10 (21.8%) UI, 2 (4.3%) IAI, 2 (4.3%) SSTI and 2 (4.3%) other infections.

Comparing the results with those of the survey

Table 3. Co-morbidity of patients

	Urinary n (%)	LTRI n (%)	ENT n (%)	IAI n (%)	AGE n (%)	SSTI n (%)	Osteoart n (%)	NRL n (%)	Flu n (%)	Total n (%)
Diabetes	416 (16.5)*	699 (19)	38 (2.3)	66 (13.7)	61 (8.9)	188 (15)	7 (17.1)	5 (20.8)	15 (5.3)	**1,510 (13.2)**
Heart disease	384 (15.3)	948 (25.8)	39 (2.3)	87 (18)	48 (7)	153 (12.2)	5 (12.2)	3 (12.5)	16 (5.7)	**1,701 (14.9)**
COPD	125 (5)	1,071 (29.1)*	23 (1.4)	26 (5.4)	18 (2.6)	60 (4.8)	2 (4.9)	1 (4.2)	12 (4.2)	**1,332 (11.7)**
Liver disease	68 (2.7)	123 (3.3)	12 (0.7)	22 (4.6)	11 (1.6)	24 (1.9)	4 (9.8)	1 (4.2)	5 (1.8)	**276 (2.4)**
CRF	162 (6.4)	244 (6.6)	5 (0.3)	24 (5)	20 (2.9)	59 (4.7)	2 (4.9)	0 (0)	4 (1.4)	**524 (4.6)**
HIV infection	10 (0.4)	51 (1.4)	6 (0.4)	2 (0.4)	7 (1)	11 (0.9)	0 (0)	2 (8.3)	6 (2.1)	**102 (0.9)**
Solid neoplasm	221 (8.8)	380 (10.3)	34 (2)	42 (8.7)	29 (4.2)	65 (5.2)	5 (12.2)	2 (8.3)	7 (2.5)	**862 (7.6)**
Blood neoplasia	37 (1.5)	88 (2.4)	9 (0.5)	2 (0.4)	12 (1.7)	13 (1)	0 (0)	0 (0)	8 (2.8)	**193 (1.7)**

LTRI: respiratory infections of lower tract; ENT: ear, nose and throat; IAI: intra-abdominal infection; AGE: gastroenteritis; SSTI: infection of skin and soft tissues; NRL: neurological; COPD: chronic obstructive pulmonary disease; CRF: chronic renal failure; *p < 0,05.

Table 4. Risk factors for poor outcome

	Urinary n (%)	LTRI n (%)	ENT n (%)	IAI n (%)	AGE n (%)	SSTI n (%)	Osteoarticular n (%)	NRL n (%)	Flu n (%)	Total n (%)
IVDU	2 (0.1)	13 (0.4)	2 (0.1)	2 (0.4)	1 (0.1)	6 (0.5)	0 (0)	0 (0)	1 (0.4)	**28 (0.2)**
Urethral probe	134 (5.3)	42 (1.1)	1 (0.1)	5 (1)	0 (0)	11 (0.9)	2 (4.9)	1 (4.2)	0 (0)	**176 (1.5)**
Institutionalized	180 (7.2)	236 (6.4)	2 (0.1)	22 (4.6)	11 (1.6)	55 (4.4)	4 (9.8)	0 (0)	1 (0.4)	**492 (4.3)**
Immunosuppression	88 (3.5)	226 (6.1)	29 (1.7)	19 (3.9)	18 (2.6)	38 (3)	3 (7.3)	1 (4.2)	14 (4.9)	**528 (4.6)**
Admission	91 (3.6)	203 (5.5)	8 (0.5)	45 (7.3)	10 (1.5)	47 (3.8)	4 (9.8)	0 (0)	6 (2.1)	**437 (3.8)**
Catheter	12 (0.5)	18 (0.5)	2 (0.1)	4 (0.8)	3 (0.4)	5 (0.4)	0 (0)	0 (0)	1 (0.4)	**57 (0.5)**
Prior AB	235 (9.3)	428 (11.6)	118 (7)	27 (5.6)	21 (3)	122 (9.8)	6 (14.6)	1 (4.2)	14 (4.9)	**1,022 (9)**

LTRI: respiratory infections of lower tract; ENT: ear, nose and throat; IAI: intra-abdominal infection; AGE: acute gastroenteritis; SSTI: infection of skin and soft tissues; NRL: neurological; IVDU: Intravenous drug user; AB: antibiotic.

in 2000[4], we observed an increase in the prevalence of infections at the EDs (14.3% vs. 10.3%; p < 0.001; RP 1.38; 95% 1, 36-1, 39) and an increase in patient age [49 (SD 22) against 53.3 (SD 23) years; p < 0.001; dif 4.30;] 95%CI 3.80-4, 80]. Regarding prevalence according to type of infection, we also found an increase in LRTI (4.6% versus 3.2%; p < 0.001; RP 1.43; 95%CI 1.40-1.47), UI (3.2% vs. 2.1%; p < 0.001; RP 1.52; 95%CI 1.47-1.56) and ENT (2.1% vs. 1.4%; p < 0.001; 1.5 RP; 95%CI 1.44-1.55). Regarding comorbidity, there is a greater number of patients with diabetes (13.2% vs. 8%; p < 0.001; RP 1.65; 95%CI 1.65-1.65), heart disease (14.9% vs. 10.2%; p < 0.001; RP 1.46; 95%CI 1.40-1.52), liver disease (2.4% vs. 1.6%; p < 0.001; 1.50 RP; 95%CI 1.33-1.67), chronic renal failure (4.6% versus 1.6%, p < 0.001; 2.88 RP; 95%CI 2.73-3.02) and neoplastic disease (9.3% vs. 3.6%; p < 0.001; RP 2.58; 95%CI 2.48-2.68). With respect to risk factors for multi-resistant microorganisms, there was a significant increase of patients on immunosuppressive therapy (4.6% versus 1.3%; p < 0.001; 3.54 RP; 95%CI 3.38-3.70 and a lower percentage of patients without any risk factor (81.1% compared to 92.5%; p < 0.001; 0.88 RP; 95%CI 0.87-0.89). Other findings included an increase of patients with septic syndrome (6.2% vs. 5.3%; p = 0. 001) 1.17 RP; 95%CI 1.07-1.27) and increased number of microbiological samples requested by ED staff (43.3% compared to 12.5%; p < 0.001; RP 3.46; 95%CI 3.42-3.51). In relation to antibiotic treatment prescribed in the EDs, we observed an increase in the use of amoxicillin-clavulanic acid (31.6% vs. 23.6%; p < 0.001; RP 1.34; 95%CI 1.30-1.38) and quinolones (23.7% vs. 18.5%; p < 0.001; RP 1.28; 95%CI 1.23-1.33). Comparative data are shown in Table 7.

Discussion

The prevalence of infection in adult patients attended in the EDs was 14.3%, an increase over the 10.4% described previously4. Similarly, we noted an increase in the prevalence of LRTI (from 3.2% to 4.6%), UI (from 2.1% to 3.2%) and ENT infection (from 1.5% to 2.1%). Possible reasons for this increase could be the increased life expectancy, longer survival of patients with neoplastic pathology or a greater number of subjects undergoing treatments involving immunosuppressive agents or biological therapies, all factors that are related with increased susceptibility to infection.

Table 5. Sepsis criteria and final destination

	Urinary n (%)	LTRI n (%)	ENT n (%)	IAI n (%)	SSTI n (%)	Osteoarticular n (%)	NRL n (%)	Total n (%)
Septic syndrome	210 (8.3)	327 (8.9)	21 (1.3)	74 (15.4)	41 (3.3)	3 (7.3)	4 (16.7)	**707 (6.2)**
Sepsis	141 (5.6)	231 (6.3)	18 (1.1)	49 (10.2)	24 (1.9)	2 (4.9)	1 (4.2)	**492 (4.3)**
Severe sepsis	46 (1.8)	60 (1.6)	3 (0.2)	17 (3.5)	11 (0.9)	1 (2.4)	3 (12.5)	**140 (1.2)**
Septic shock	23 (0.9)	36 (1)	0 (0)	8 (1.7)	6 (0.5)	0 (0)	0 (0)	**75 (0.7)**
Destination								
OBS	222 (8.8)	367 (10)	29 (1.7)	47 (9.8)	51 (4.1)	0 (0)	1 (4.2)	**812 (7.1)**
SSU	50 (2)	127 (3.5)	2 (0.1)	8 (1.7)	11 (0.9)	0 (0)	0 (0)	**209 (1.8)**
Med	413 (16.4)	1,271 (34.6)	68 (4.1)	216 (44.8)	163 (13)	18 (43.9)	19 (79.2)	**2,280 (20)**
SUR	5 (0.2)	0 (0)	6 (0.4)	173 (35.9)	119 (9.5)	4 (9.8)	0 (0)	**314 (2.8)**
UCI	7 (0.3)	35 (1)	2 (0.1)	7 (1.5)	3 (0.2)	0 (0)	4 (16.7)	**59 (0.5)**
Discharge	1,810 (71.9)	1,848 (50.2)	1,571 (93.6)	29 (6)	901 (72.1)	19 (46.3)	0 (0)	**7,679 (67.4)**
Death	10 (0.4)	30 (0.8)	0 (0)	2 (0.4)	2 (0.2)	0 (0)	0 (0)	**46 (0.4)**

LTRI: respiratory infections of lower tract; ENT: ear, nose and throat; IAI: intra-abdominal infection; AGE: gastroenteritis; SSTI: infection of skin and soft tissues; NRL: neurological; OBS: observation; SSU: short stay unit: Med: medicine; SUR: surgery; ICU: intensive care unit.

Table 6. Antibiotics used in the Emergency Department

	Urinary n (%)	LTRI n (%)	ENT n (%)	IAI n (%)	Enteritis n (%)	SSTI n (%)	Osteoart n (%)	NRL n (%)	Total n (%)
Quinolones	640 (25.4)	1,608 (43.7)	191 (11.4)	30 (6.2)	93 (13.5)	99 (7.9)	10 (24.4)	0 (0)	**2,704 (23.7)**
Moxifloxacin	5 (0.2)	236 (6.4)	30 (1.8)	0 (0)	0 (0)	2 (0.2)	0 (0)	0 (0)	**274 (2.4)**
Levofloxacin	107 (4.3)	1,324 (36)	27 (1.6)	3 (0.6)	3 (0.4)	26 (2.1)	2 (4.9)	0 (0)	**1,503 (13.2)**
Ciprofloxacin	528 (21)	48 (1.3)	134 (8)	27 (5.6)	90 (13.1)	71 (5.7)	8 (19.5)	0 (0)	**927 (8.1)**
Beta-Lactam	1,263 (50.2)	1,459 (39.7)	1,020 (60.8)	238 (49.4)	15 (2.2)	840 (67.2)	20 (48.8)	16 (66.7)	**5,171 (45.4)**
Amox/Amp	22 (0.9)	54 (1.5)	103 (6.1)	2 (0.4)	1 (0.1)	19 (1.5)	0 (0)	6 (25)	**222 (1.9)**
Amox-clav	666 (26.5)	1,003 (27.3)	815 (48.6)	90 (18.7)	5 (0.7)	761 (60.9)	11 (26.8)	1 (4.2)	**3,600 (31.6)**
Cephalosporin 2 G	220 (8.7)	43 (1.2)	77 (4.6)	10 (2.1)	0 (0)	14 (1.1)	1 (2.4)	0 (0)	**369 (3.2)**
Ceftriaxone	335 (13.3)	261 (7.1)	21 (1.3)	46 (9.5)	4 (0.6)	30 (2.4)	7 (17.1)	12 (50)	**722 (6.3)**
Ceftazidime	11 (0.4)	23 (0.6)	4 (0.2)	1 (0.2)	0 (0)	1 (0.1)	0 (0)	0 (0)	**50 (0.4)**
Cefepime	3 (0.1)	23 (0.6)	2 (0.1)	1 (0.2)	0 (0)	0 (0)	1 (2.4)	1 (4.2)	**41 (0.4)**
PPR/TAZ	26 (1)	61 (1.7)	0 (0)	95 (19.7)	5 (0.7)	16 (1.3)	1 (2.4)	0 (0)	**208 (1.8)**
Macrolide	18 (0.7)	175 (4.8)	65 (3.9)	0 (0)	2 (0.3)	11 (0.9)	0 (0)	0 (0)	**286 (2.5)**
Carbapenemico	62 (2.5)	76 (2.1)	2 (0.1)	91 (18.9)	2 (0.3)	40 (3.2)	0 (0)	0 (0)	**276 (2.4)**
Imipenem	40 (1.6)	55 (1.5)	1 (0.1)	27 (5.6)	0 (0)	19 (1.5)	0 (0)	0 (0)	**148 (1.3)**
Ertapenem	22 (0.9)	21 (0.6)	1 (0.1)	64 (13.3)	2 (0.3)	21 (1.7)	0 (0)	0 (0)	**128 (1.1)**
Metronidazole	5 (0.2)	12 (0.3)	25 (1.5)	62 (12.9)	8 (1.2)	25 (2)	0 (0)	0 (0)	**138 (1.2)**
Clindamycin	4 (0.2)	22 (0.6)	17 (1)	3 (0.6)	0 (0)	46 (3.7)	1 (7.3)	0 (0)	**113 (1)**
Aminoglycoside	64 (2.5)	24 (0.7)	12 (0.7)	6 (1.2)	1 (0.1)	11 (0.9)	4 (9.8)	2 (8.3)	**262 (2.3)**
Glycopeptide	9 (0.4)	9 (0.2)	0 (0)	3 (0.6)	0 (0)	8 (0.6)	5 (12.2)	4 (16.7)	**47 (0.4)**
Linezolid	1 (0)	5 (0.1)	0 (0)	1 (0.2)	0 (0)	4 (0.3)	2 (4.9)	0 (0)	**14 (0.1)**
Tigecycline	0 (0)	0 (0)	0 (0)	1 (0.2)	0 (0)	2 (0.2)	0 (0)	0 (0)	**4 (0)**
Without treatment	73 (2.9)	489 (13.3)	307 (18.3)	109 (22.6)	558 (81)	153 (12.2)	8 (19.5)	6 (25)	**2,110 (18.5)**

SD: standard deviation; LTRI: respiratory infections of lower tract; ENT: ear, nose and throat; IAI: intra-abdominal infection; AGE: gastroenteritis; SSTI: infection of skin and soft tissues; Osteoart: osteo-articular; NRL: neurological; *p < 0.05; 2 G: second generation; PPR/TAZ: piperacillin/tazobactam.

The increase in life expectancy is also reflected in mean age of the population studied, which showed a significant increase with respect to that published previously, from 49 years (SD 22) to 53 years (SD 23). Although the largest number of infections was associated in the past to young patients with immune disorders, at present the vast majority of infections occur in elderly patients. These data are related to frequent comorbidity, increased age and the physiological changes of aging that make elderly patients more vulnerable to infectious processes[10,11].

Underlying diseases collected reflect those most prevalent in the general population, with a reduction of pathology associated with infection by HIV or COPD and an increase of neoplastic pathology, liver disease, chronic renal failure, diabetes and heart disease in our work, similar to previous studies[4,12]. In relation to the factors of selection of multiresistant pathogens, we would highlight the percentage of patients with some degree of immunosuppression, consistent with the characteristics of the patients we serve[3,13]. Also the fact that one in ten patients was taking antibiotics when it attended at the ED (in a similar percentage to that reported in 2000), that the percentage of institutionalization was 4.3%, and 3.8% of the patients had been admitted in the month before attention at the EDs.

The percentage of patients without co-morbidity attended for an infectious process decreased with regard to the previous study (59.4% vs. 50.4%), as well as those without associated risk factors (92.5% vs. 81.1%). Both circumstances could eventually condition the selection of multiresistant pathogens since these cases present a greater number of infectious episodes, followed by their corresponding cycles of antimicrobials that could select their flora, even in patients from the community[5,7]. In fact, although infection by multi-resistant microorganisms has typically been associated with nosocomial infections, there are increasingly more frequent publications that refer to an increase of these pathogens in patients with community-acquired infection. Considering the scarcity of rapid diagnostic microbiological techniques and the increase in survival that occurs with adequate empiric antibiotic treatment[14], the ED physician faces a new challenge in antibiotic prescribing, and must identify patients with risk factors associated with infection by multiresistant pathogens and decide, based on these and the model of infection, the antimicrobial strategy. All these data confirm, on the one hand, the importance and the impact of infections in the daily work of EDs and, on the other hand, the progressive increase in age and complexity of patients attended there, which is constant in our environment and requires better training in the detection of these factors of selection by ED staff regarding antibiotic treatment[15].

Table 7. Results of both epidemiological studies (2000. register 1. and 2012. register 2)

	Register 1 (n = 16.152)	Register 2 (n = 11.399)		
Variable	**No. cases (%)**	**No. cases (%)**	**RP* (95% CI)**	***p***
Age (years) [mean (SD)]	49 (22)	53 (23)	4.30 (3.80-4.80)	< 0.001
Sex (male)	856 (53)	5,563 (48.8)	0.92 (0.90-0.94)	< 0.001
Comorbidity				
COPD	2,681 (16.6)	1,332 (11.7)	0.70 (0.64-0.77)	< 0.001
Heart disease	1,647 (10.2)	1,701 (14.9)	1.46 (1.40-1.52)	< 0.001
Diabetes	1,292 (8)	1,510 (13.2)	1.65 (1.65-1.65)	< 0.001
Liver disease	258 (1.6)	276 (2.4)	1.50 (1.33-1.67)	< 0.001
CRF	258 (1.6)	524 (4.6)	2.88 (2.73-3.02)	< 0.001
HIV infection	355 (2.2)	102 (0.9)	0.41 (0.19-0.63)	< 0.001
Neoplasia	581 (3.6)	1,055 (9.3)	2.58 (2.48-2.68)	< 0.001
Without comorbidity	9,594 (59.4)	5,744 (50.4)	0.85 (0.82-0.87)	< 0.001
Risk factors				
Intravenous drug use	275 (1.7)	28 (0.2)	0.12 (–0.27-0.51)	< 0.001
Bladder probe	242 (1.5)	176 (1.5)	1 (–0.19-0.19)	0.759
Immunosuppression	210 (1.3)	528 (4.6)	3.54 (3.38-3.70)	< 0.001
Prior AB	1,502 (9.3)	1,022 (9)	0.97 (0.89-1.04)	0.344
No risk factors	14,941 (92.5)	9,243 (81.1)	0.88 (0.87-0.89)	< 0.001
Sepsis	856 (5.3)	707 (6.2)	1.17 (1.07-1.27)	0.001
Microbiology	2,019 (12.5)	4,936 (43.3)	3.46 (3.42-3.51)	< 0.001
Admission	3,327 (20.6)	2,653 (23.3)	1.13 (1.08-1.17)	< 0.001
Type of infection				
Urinary	3,481 (21.5)	2,517 (22.1)	1.03 (0.98-1.07)	0.294
Respiratory	5,288 (32.7)	3,678 (32.3)	0.99 (0.95-1.02)	0.409
ENT	2,190 (13.6)	1,678 (14.7)	1.08 (1.03-1.14)	0.006
SSTI	2,843 (17.6)	1,250 (11)	0.63 (0.56-0.69)	< 0.001
Digestive	4,458 (27.6)	1,171 (10.2)	0.37 (0.31-0.43)	< 0.001
Antibiotic				
Amoxicillin-clavulanic acid	3,812 (23.6)	3,600 (31.6)	1.34 (1.30-1.38)	< 0.001
2nd generation cephalosporin	1,163 (7.2)	369 (3.2)	0.44 (0.33-0.56)	< 0.001
3rd generation cephalosporin	1,421 (8.8)	772 (6.7)	0.76 (0.68-0.85)	< 0.001
Macrolides	1,971 (12.2)	286 (2.5)	0.20 (0.08-0.33)	< 0.001
Quinolones	2,988 (18.5)	2,704 (23.7)	1.28 (1.23-1.33)	< 0.001
Without AB	3,085 (19.1)	2,110 (18.5)	0.97 (0.92-1.02)	0.218

RP: rate of prevalence; COPD: chronic obstructive pulmonary disease; CRF: chronic renal failure; IVDU: Intravenous drug user; AB: antibiotic; ENT: ear, nose and throat; SSTI: skin and soft tissue infection.

The predominance of LRTI over the rest of the infections has been known for many years, both in seasonal variation and characteristics[16,17]. The prototype of the respiratory infection patient remains as males with higher than average age and a history of COPD, as well as the predominance of pulmonary bronchial infections. UI occurred most frequently in women of childbearing age, mainly cystitis. UI patients also had a number of predisposing factors such as the nephropathy, diabetes mellitus, or the presence of a permanent urinary catheter. These results are consistent with those published by other authors[18-20], who identified as risk factors for UI, in addition to those mentioned above, catheter bearers or immunodeficiency. Conversely, ENT infections were mainly found in younger patients, usually without underlying diseases or risk factors for infections; the predominant picture was sore throat and, in general, less serious infections. They are infections frequently treated in primary care, in accordance with their clinical features, and incidence is even higher in the age range of 3-15 years[21], an age group not included in the present study (> 14 years).

IAI comprised heterogeneous clinical entities which hinders uniform data analysis. The topographic distribution of the conditions in the abdomen, frequently in patients over 30 years of age, the prevalence in men, the presence of sepsis in one of every 5 patients and the rate of admission for one of every two are similar to data previously reported[22,23]. SSTI did not present important features or major differences compared to the rest of the infections and to what is already known[24,25]. Non-necrotizing infections predominated with amoxicillin-clavulanic acid as the antimicrobial used in two thirds of cases, without remarkable differences with other series[26]. Joint infections accounted for a small percentage of the total which hinders drawing conclusions. Neurological infections presented a high index of severity of sepsis, rates of antimicrobial use and admission criteria, as corresponds to these clinical pictures[27].

The miscellaneous section includes a wide variety of infectious, non-relevant processes individu-

ally, but which globally are not negligible. The treatment of these processes is beyond the scope of EDs, and they should therefore be analyzed in other studies.

In relation to the criteria for sepsis, fulfilled in 6.2% of the patients, a slight increase over previous reports was found[4], consistent with increasing age, comorbidity, and risk factors. This increase may be related to better identification of patients with sepsis, as a result of training campaigns conducted in recent years. However, due to the absence of an appropriate source of all constants or the increasingly common presence of patients with immunosuppression or advanced age, where the clinical signs and symptoms are mild and hinder their proper identification, their frequency may be underestimated in EDs. In this regard, the use of biomarkers of acute infection such as procalcitonin may be very useful for early identification and clinical decision-making, both in terms of care location and therapeutic strategy[28,29]. Sepsis predominated, and criteria for severe sepsis or septic shock were rare. Community-acquired pneumonia, pyelonephritis, intra-abdominal and the CNS infection presented the highest rate of sepsis, with more than 20%, which is consistent with data published in the literature[30-32].

Regarding microbiological studies, none were requested for more than half the patients. This is common and reflects the system of work in EDs[33,34], where diagnoses are usually presumptive, based on clinical history and basic complementary examinations, so antibiotic treatment is almost always empirical[35]. However, compared with the previous epidemiological study, there was a significant increase in application (12.5% vs. 43.3%). This could reflect a greater awareness by ED physicians as to the importance of microbiology results for subsequent targeted therapy, (if necessary), and decrease mortality rates[14], or to adapt treatment as a control measure against the selection of bacteria that are resistant, by reduced antibiotic pressure[36]. In this regard, we would emphasize the need to maintain fluent communication with primary care staff, bearing in mind that 67% of patients attended for infection in the EDs are discharged and directed to primary health care without knowing the result of the cultures performed.

With respect to antibiotic treatment, the use of amoxicillin-clavulanic acid remained dominant, followed by cephalosporins and fluoroquinolones. The latter were most frequently used in patients with sepsis criteria, probably because LRTI are the leading cause of sepsis, and fluoroquinolones are standard for that model of infection.

With respect to the previous study, we would highlight the decreasing use of macrolides in LRTI and ENT infection. Reports on increased resistance to macrolides by the main respiratory pathogens possibly explain this low use. In LRTI there was also a decline in the use of amoxicillin-clavulanic acid (27.3% versus 29.9% in 2000) and cephalosporins (10.3% vs. 30.4% in 2000) in favour of quinolones, which coincides with the publication of numerous treatment guidelines in the last decade.

We observed a decrease in the use of aminoglycosides for UI and, on the other hand, increased prescription of quinolones, despite the high rate of resistance described for e. coli (over 30%), the main etiologic agent of these infections. It is true that its use was much lower than a decade ago (67.3% versus 25.4% today), but then there were no sensitivity problems.

There has been also an increase in the prescription of carbapenems for IAI compared with the year 2000, which may be related with the emergence of ertapenem, a drug of this therapeutic group without antipseudomonal activity with good cover against community organisms. This rise in the prescription of carbapenem for IAI is lower than in other series[37]. Finally, in the comparative analysis with the epidemiological study of the year 20004, it is also remarkable that the number of patients not prescribed antibiotic treatment is similar (18.5% versus 19.1%), despite increasing age and co-morbidity risk factors observed during the last decade.

The interpretation of these data is not straightforward. In the case of ENT infection, frequently of viral origin, adding an antibiotic would not be justified. The same applies to some cases of acute bronchitis or summer gastroenteritis. In the case of neurological infection, viral encephalitis should of course not be treated with antibiotics but rather antiviral drugs. On some occasions, antimicrobial treatment is initiated elsewhere (other than in EDs) for various reasons. Such is the case with IAI or surgical bone infection, when antibiotics may even be initiated in the operating room. More difficult to explain is the absence of treatment for UI, where we found patients who were untreated or treated with inappropriate antibiotics (e.g. macrolides). This is the best justification for the elaboration of protocols, sessions and practice guidelines by scientific societies.

Regarding patient care destination, 20% were admitted to medical specialties, 23.3% if we include the ICU and surgery. This is higher than general admission rates and those reported in the

study published in the 2000[4], but this is justified by the increased complexity and severity of the patients currently attended in the ED. Regarding this point, the existence of observation units and short stay units enables better utilization of health resources38, where 8.9% of patients are cared for, becoming the second leading destination of patients not receiving hospital discharge.

Comparing the results of this study with others also assessing patients who visit the ED for infection, but in other environments, our study showed a strikingly lower number of admissions to hospital and ICU and deaths, reported as 80%, 7% and 3.5%, respectively[39,40]. This discrepancy may be due to differences in the design of the studies. Both were single-center studies including patients only according to the presence of fever greater than 38°C, while in our case they were included according to the clinical judgment of the physician that attended them. In this respect, we would mention that patients do not always present with high temperature, either because they are immunosuppressed or have previously taken an antipyretic before consulting the ED. Another factor to consider is the cut-off point for the denomination of fever in the elderly patient, a numerically significant population in EDs, as tympanic temperature of 37.2°C[41], an issue not considered in the two studies cited above. Finally, around 4-22% of patients who consult for fever do not present a picture of infection[42]. These factors can condition greater severity of patients analyzed, increasing the number of admissions to conventional hospitalization and the ICU. On the other hand, these studies evaluated mortality during the whole hospital admission, while we only considered deaths occurring in the EDs.

Sampling with multiple nationwide hospitals within such a narrow time frame entails certain limitations in terms of diagnostic and even therapeutic criteria. In this study, the INFURGSHEMESH working group recorded the diagnosis issued by the clinician who attended the patient in his/her clinical report, and therefore assumed the margin of error generated by the pathogenesis of certain diseases (e.g. pericarditis, appendicitis, etc.) and the inter-individual variability in qualitative variable data.

In conclusion, infectious diseases account for a high percentage of ED care work and their prevalence has increased in the last decade. LRTI, UI and ENT infections continue to be the most frequent types of infection. There was an increase in severity of these processes, evidenced by the increase in patients suffering from sepsis on arrival at the ED. The increases observed in prevalence, age, co-morbidity and factors of selection of resistant microorganisms paint a different profile of the infected patient attended in the ED compared to the data published in the last decade, reflecting greater complexity of infectious processes, and this can hinder the diagnosis, evaluation and proper management of these patients in the ED.

Addendum

Other members of the INFURGSEMES group are as follows: Teresa Soriano (Hospital Vall d'Hebron), Carlos Herráiz de Castro (Hospital Virgen de la Luz), Sergio Navarro (Hospital de Alzira), Ana Álvarez (Hospital Mutua de Terrassa), Pablo Marchena (Hospital Sant Joan de Déu de Sant Boi de Llobregat y Hospital Moisés Broggi de Sant Joan Despí), Verónica Díez (Hospital de la Santa Creu i Sant Pau), Zita Quintela (Hospital 12 de Octubre), Cristina Urdánoz (Hospital Virgen del Camino), Nikole Velilla (Hospital de Navarra), María Sada (Hospital García Orcoyen), Julián Mozota (Hospital Clínico Lozano Blesa), María Ángeles Leciñena (Hospital Can Misses), Elena Díaz (Hospital de San Juan), Carmen Capdepon (Hospital Los Arcos), Ramón Perales (Hospital General Albacete), Juan Sánchez (Hospital Virgen de las Nieves), Coral Suero (Hospital Clínico de Málaga), Octavio Salmerón (Hospital Fundación Alcorcón), Carmen del Arco (Hospital de La Princesa), Beatriz Valle (Hospital Severo Ochoa), Francisco Javier Martín Sánchez (Hospital Clínico San Carlos), Esther Díaz (Hospital Puerta de Hierro), Javier Oñate (Hospital Universitario de Cruces), Miguel Ortega (Hospital de Galdakao), Manuel Fernández (Hospital San Eloy), Itziar Huarte (Hospital Donosti), Alejandro Juan Masie (Hospital Alto Deba), Carmen Andonegui (Hospital Mendaro), Reyes Yagüe (Hospital Txagorritxu), Dolores Carrión (Hospital Comarcal Mora d'Ebre), Salvador Sarrá (Hospital del Vendrell), Silvia Flores (Hospital Santa Tecla), Carmen Boqué (Hospital Universitari Joan XII), David Rodríguez (Hospital Comarcal d'Amposta), Cinta Saiz (Hospital Municipal de Badalona), Luis Lapuerta (Hospital Santa Bárbara), María José Antequera (Hospital El Bierzo), María Carmen Rivas (Hospital Virgen del Castañar), Jorge García (Hospital Clínico de Salamanca), Agustín Arévalo (Hospital Virgen de la Vega), Raúl López (Hospital Río Hortega), Ana Isabel Carazo (Hospital Río Carrión), Sebastián Martínez (Hospital Virgen de la Concha), Carlos Avellaneda (Hospital de Segovia).

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Estudio INFURG-SEMES: epidemiología de las infecciones atendidas en los servicios de urgencias hospitalarios y evolución durante la última década

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Objetivos: Estudiar la prevalencia de las enfermedades infecciosas, así como el perfil y el manejo de los pacientes con clínica de infección en los servicios de urgencias hospitalarios (SUH) españoles y valorar su evolución en los últimos años al compararlo con un estudio previo publicado hace 12 años.
Método: Estudio descriptivo multicéntrico con análisis transversal llevado a cabo en 49 SUH españoles los días 10 y 20 de cada mes durante un periodo de 12 meses. Para el cálculo de la prevalencia, se registraron el número de pacientes con diagnóstico clínico de infección, así como su localización y el número total de atenciones durante el periodo del estudio. Para el estudio del perfil y manejo de los pacientes, se recogieron las características sociodemográficas, las enfermedades asociadas, los factores de riesgo para patógenos multirresistentes, los estudios microbiológicos solicitados, el tratamiento antimicrobiano prescrito, el destino final y la mortalidad en urgencias.
Resultados: La prevalencia de enfermedades infecciosas en los SUH fue del 14,3% (4,6% respiratoria, 3,2% urinaria, 2,1% otorrinolaringológica, 1,6% infecciones de piel y partes blandas –IPPB– y 2,8% otras); 4.543 (39,8%) presentaban enfermedades asociadas como la diabetes mellitus, cardiopatía o enfermedad pulmonar obstructiva crónica; y 707 (6,2%) cumplían criterios de sepsis a su llegada a urgencias. Respecto al manejo, no se realizó estudio microbiológico en 6.463 (56,7%) pacientes, y la amoxicilina-clavulánico fue el antibiótico más frecuentemente prescrito (3.600 casos, 31,6%). Un total de 1.022 (9%) pacientes ya estaban tomando tratamiento antibiótico cuando consultaron en urgencias. Respecto a la evolución, 46 (0,5%) pacientes fallecieron en urgencias y 2.653 (23,3%) fueron hospitalizados.
Conclusiones: La atención de las enfermedades infecciosas supone un porcentaje relevante en la labor asistencial desarrollada en los SUH españoles, especialmente las infecciones respiratorias y urinarias. Al comparar los resultados con el estudio previo, se observa un aumento en la prevalencia de las infecciones, con un perfil de pacientes de mayor edad, comorbilidad, factores de riesgo de microorganismos multirresistentes y síndrome séptico. [Emergencias 2013;25:368-378]

Palabras clave: Infecciones. Epidemiología. Servicio de urgencias. Antibióticos. Mortalidad. Sepsis. Bacteriemia.