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# In-hospital mortality due to infectious disease in an Internal Medicine Department. Epidemiology and risk factors

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**Abstract. – OBJECTIVE: Hospital mortality is a leading indicator of quality of healthcare and a valuable tool for planning and management. Infectious diseases represent a substantial part of the activity of internal medicine.Our aim was to describe the characteristics of in-hospital mortality due to infectious diseases and associated risk factors in our environment.**

**MATERIALS AND METHODS: A retrospective case-control study was designed. We reviewed deaths during 2012 from an Internal Medicine Department. 187 cases (infectious disease related mortality) and 224 controls were found. Clinical and demographic information was obtained from medical records. Comorbidity was evaluated with Charlson index (CI). Data were analyzed using SPSS 15.0 ($p$-value < 0.05).**

**RESULTS: During 2012, of the 3193 discharge, 187 were exitus due to infectious disease (5.8%). Mean age was 85.7 ± 7.6, higher in women (88 ± 7 vs 83 ± 7.4, $p < 0.001$), and 55% were aged over 85 years. The CI mean was 4.2 ± 3, higher in younger than 85 years (5.3 ± 3.4 vs 3.6 ± 2.6, $p < 0.001$). Most frequent causes of death were respiratory sepsis (29%), severe pneumonia (23.5%) and urinary sepsis (16.6%) and risk factors were living in Nursing Home (55.6% vs 34%, $p < 0.001$), being dependent (73.8% vs. 44.6%, $p < 0.001$), dementia (59.4% vs 27.2%, $p < 0.001$) and cerebrovascular disease (25.7% vs 17.4%, $p = 0.041$).**

**CONCLUSIONS: Dementia, cerebrovascular disease, living in Nursing Home and being dependent were risk factors for infectious disease in-hospital mortality in our study, but not comorbidity, age or length of stay. Our series, although limited by retrospective design, is the first qualitative study of in-hospital mortality due to infectious disease in an Internal Medicine Service in our environment. Most frequent cause of death in our setting was respiratory etiology.**

*Key words:*
Infectious disease, In-hospital mortality, Internal Medicine, Quality of care, Elderly.

## Introduction

Infectious diseases represent a substantial part of the care activity of Internal Medicine Services, with studies showing that up to 30% of all admissions are due to infections[1-3].

Despite continuous advances in treatment, recent epidemiological and microbiological changes have led to an increase in morbidity and mortality caused by infection, with a consequent increase in the use of health care resources[4-6]. In addition, in developed countries, the aging population and increased life expectancy have increased hospital use due to comorbidities and the need for a global approach to them[7-9].

In-hospital mortality is a leading indicator of the quality of healthcare and its analysis is a valuable tool for planning and management. Likewise, evaluation of hospital deaths may be used to measure the effectiveness of hospital care[8,10]. Recent data from the World Health Organization show infectious diseases are the first cause of death in 27.5% of all deaths worldwide, corresponding to more than 15 million people annually[11]. Infectious diseases are the second category of cause of death in Internal Medicine Services in Spain[12].

Although studies have evaluated global mortality in Internal Medicine services in recent years[12-14], there are no Spanish studies on the specific epidemiology of mortality due to infectious diseases. Therefore, the aim of our study was to

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describe the characteristics of deaths due to infectious disease in our department, to identify associated risk factors and compare them with those of deaths due to non-infectious causes.

## Material and methods

We retrospectively studied all deaths in 2012 in the Internal Medicine Service of Rio Hortega University Hospital of Valladolid, which serves a population of approximately 250 000. Sociodemographic and clinical information was obtained from digitalized medical records and risk factors for death due to infectious disease were evaluated. The following variables were collected:

- Sociodemographic factors: age, sex, usual residence.
- Chronic conditions: Diabetes mellitus (DM), arterial hypertension (HT), chronic renal disease (CRD), neoplasms, cardiopulmonary disease, cerebrovascular disease, cognitive impairment and dependence.
- Hospital admission in the month before death, hospital attendance (defined as hospital admittance in the previous year), reason for admission, length of stay, end-of-life situations, primary cause of death (and secondary if recorded) and early mortality (within 48 hours after admission).
- Quality of care of deaths: foreseeable deaths, do-not-resuscitate orders and palliative treatment.
- Complementary information: fever at admission (temperature > 38°C), nosocomial fever, hypotension at admission (systolic blood pressure < 90 mmHg), complications during admission, obtention of microbiological samples (blood, urine, and sputum cultures, rapid detection of antigens in urine and other samples) and outcomes of then and use of antibiotic treatment (empiric therapy and fitting with the antibiogram).

The original version of the Charlson Index (CI) was used to assess comorbidity. The CI is a scale consisting of 19 items corresponding to comorbidities which, due to their severity, are risk factors for increased mortality. Each item is assigned a score of 1, 2, 3 or 6 according to the associated risk of mortality. The sum of all items provides a total score which predicts mortality: 0-1 points indicates no comorbidity, 2 points low comorbidity and 3 points high comorbidity. This yields an index that predicts short-term (< 3 years) mortality: 0 = 12% mortality/year, 1-2 = 26%, 3-4 = 52%, and >5 = 85%, as previously described [15].

*Case* was defined as a death due to infectious causes (specified as such in the medical record by the attending physician according to clinical parameters and the results of appropriate additional studies). *Control* was defined as a death due to noninfectious etiology.

### Statistical Analysis

The characteristics of the study sample were described as mean ± standard deviation, frequencies and percentages. We analyzed associations between variables using the chi-square test and differences between means using the Student *t* test and ANOVA. Data were analyzed using the SPSS 15.0 (SPSS Inc., Chicago, IL, USA) statistical package. Level of statistical significance was established as $p \leq 0.05$.

## Results

In 2012, there were 3193 discharges from our Internal Medicine Service, of which 411 (12.8%) were deaths. Of these, 45.5% (N = 187) were identified as cases (death caused by infection) and 54.5% (N = 224) as controls (death due to noninfectious causes). Global mortality due to infections was 5.8%.

Of cases, 48% were male. Mean age was 85.7 ± 7.6 years (range 57-102), which was higher in females (88 ± 7.3 vs. 85 ± 7.4, $p < 0.001$): 55% were aged > 85 years. The mean CI score was 4.2 ± 3 (range 0-13), and was higher in patients aged < 85 years (3.7 ± 2.7 vs. 4.7 ± 3, $p = 0.018$). Comorbidity was high (more than 2 points) in 68.4% (N = 128) of cases, and also was more frequent in younger patients (79.8% vs. 59.2%, $p = 0.01$). Other data are shown in Table I.

The mean hospital stay was 9 ± 9 days, with no differences according to age or sex. The main reasons for admission were infectious disease (56%, N = 105), cardiopulmonary disease (17.6%, N = 33), bronchoaspiration (8%, N = 15), gastrointestinal disorders (7%, N = 13) and malaise (7%, N = 13). 47.6% (N = 89) of patients were admitted in an end-of-life situation. During the hospital stay, 8.6% (N = 16) of patients had bronchoaspiration and nosocomial pneumonia was detected in 5.3% (N = 10). A total of 18.2% (N = 34) of patients had been hospitalized in the previous 30 days and 53% (N = 99) in the previous year, with no differences according to age or sex.

**Table I.** Sociodemographic, epidemiological and clinical characteristics of patients dying from infectious causes and patients dying from non-infectious causes.

| | Death due to infectious causes N=187 (%) | Death due to non-infectious causes N=224 (%) | *p*-value |
|---|---|---|---|
| Female | 97 (52) | 122 (54.5) | 0.600 |
| Mean age (SD), years | 85.7 ± 7.6 | 84.4 ± 9.9 | 0.121 |
| Age > 85 years | 103 (55) | 127 (56.7) | 0.742 |
| Usual residence | | | |
| Geriatric center | 104 (55.6) | 76 (34) | **< 0.001** |
| Clinical history | | | |
| Hypertension | 119 (63.6) | 171 (76.3) | **0.005** |
| Myocardial infarction | 29 (15.5) | 52 (23.2) | **0.050** |
| Heart failure | 76 (40.6) | 104 (46.4) | 0.239 |
| Diabetes mellitus | 50 (26.7) | 61 (27.2) | 0.500 |
| Cerebrovascular disease with sequelae | 48 (25.7) | 39 (17.4) | **0.041** |
| Chronic respiratory disease | 52 (27.8) | 69 (30.8) | 0.506 |
| Chronic renal disease | 41 (22) | 58 (26) | 0.349 |
| Neoplasm without evidence of metastasis | 30 (16) | 39 (17.4) | 0.407 |
| Neoplasm with metastasis | 13 (7) | 37 (16.5) | **0.003** |
| Chronic liver disease | 2 (1.1) | 8 (3.6) | 0.091 |
| Leukemia | 3 (1.6) | 4 (1.8) | 0.598 |
| Lymphoma | 2 (1.1) | 6 (2.7) | 0.209 |
| AIDS | 3 (1.6) | 0 (0) | **0.050** |
| Cognitive impairment | 111 (59.4) | 61 (27.2) | **< 0.001** |
| Dependency for ADL | 138 (73.8) | 100 (44.6) | **< 0.001** |
| Charlson index (mean score, SD) | 4.2 ± 3 | 4.5 ± 3.2 | 0.279 |
| Charlson index (groups) | | | 0.839 |
| No comorbidity | 31 (16.6) | 38 (17) | |
| Low comorbidity (score 2 points) | 28 (15) | 29 (13) | |
| High comorbidity (score > 2 points) | 128 (68.4) | 157 (70) | |
| Predicted mortality according to Charlson index | | | 0.346 |
| Score 0 (12% mortality/year) | 6 (3.2) | 14 (6.3) | |
| Score 1-2 (26% mortality/year) | 53 (28.3) | 53 (23.7) | |
| Score 3-4 (54% mortality/year) | 59 (31.5) | 66 (29.5) | |
| Score ≥ 5 (85% mortality/year) | 69 (37) | 91 (40.5) | |
| Hospital admission in previous year | 99 (53) | 134 (59.8) | 0.097 |
| Hospital admission in previous 30 days | 34 (18.2) | 45 (20) | 0.359 |
| Hospital stay (days) | 9 ± 9 | 8 ± 8 | 0.242 |
| Early mortality | 44 (23.5) | 62 (27.7) | 0.199 |
| End-of-life situation at admission | 89 (47.6) | 122 (54.5) | 0.099 |
| Quality of care of deaths | | | |
| Register of foreseeable death | 169 (90.4) | 190 (84.8) | 0.061 |
| Do-not-resuscitate order | 153 (82) | 177 (79) | 0.279 |
| Palliative treatment | 142 (76) | 163 (72.8) | 0.269 |

SD: standard deviation; ADL: activities of daily living.

The leading causes of death were respiratory sepsis (29%, N = 54), severe pneumonia (23.5%, N = 44), urological sepsis (16.6%, N = 31) and abdominal sepsis (6.4%, N = 12). In 76.5% (N = 143) of patients, a secondary cause of death was recorded, including respiratory failure (38%, N = 54), acute heart failure (HF) (12.6%, N = 18), and advanced CRD (7.7%, N = 11). 23.5% (N = 44) of deaths occurred in the first 48 hours after admission. With respect to the quality of care in deaths, foreseeable death was recorded in 90.4% of cases (N = 169), no-resuscitation-orders were issued in 82% (N = 153) and palliative treatment was administered in 76% (N = 142), with no differences according to age or sex.

Infection-related symptoms at hospital admission included hypotension in 38% (N = 71) of

cases while 52.4% of cases (N = 98) had fever, which was more frequent in patients aged < 85 years (60.7% vs. 45.6%, $p = 0.04$). Thirteen per cent of cases (N = 25) developed nosocomial fever during hospital stay. With respect to microbiological diagnostic techniques, blood cultures were collected in 52% (N = 97) of cases, of which 16.5% (N = 16) were positive, urine in 40.6% (N = 76), of which 39.5% (N = 16) were positive, sputum in 6% (N = 11) of which 54.5% (N = 6) were positive, and qualitative antigenuria for *pneumococcus* and *Legionella* in 14. 4% (N = 27), of which 15% (N = 4) were positive for *pneumococcus* and 3.7% (N = 1) for *Legionella*. Empirical antibiotic therapy was administered in 81% (N = 151) of cases and no antibiotic treatment was administered in 19% of cases (N = 36). Empirical antibiotic therapy was not changed in 71.5% (N = 107) of cases: this was to death before the microorganism involved was identified, no isolation from microbiological samples or failure to obtain samples. Antibiotic therapy was changed in 19.2% (N = 29) of cases and was the correct therapy according to the antibiogram in 9.3% (N = 14) of cases. The characteristics of patients who died of infectious and non-infectious causes are compared in Table I.

Our patients were predominantly aged > 85 years and female, with no significant differences between cases and controls. However, deaths due to infectious disease were significantly more frequent in patients living in geriatric centers (55.6% vs. 34%, $p <0.001$) and in patients with a history of cerebrovascular disease with sequelae (25.7% vs. 17.4%, $p = 0.041$), cognitive impairment (59.4% vs. 27.2%, $p <0.001$) and dependency for activities of daily living (73.8% vs. 44.6%, $p < 0.001$), but not in patients with other conditions that may compromise immunity, such as CRD, DM, liver disease, solid tumors of any grade, leukemia and lymphomas. In contrast, a history of cardiovascular involvement, such as HT or chronic ischemic heart disease, were inversely associated with death due to infectious disease (63.3% vs. 76.3%, $p = 0.005$ and 15. 5% vs. 32.2%, $p = 0.05$, respectively). The mean CI score and the CI categories, greater hospital attendances, and the length of hospital stay, were not associated with deaths due to infectious disease. With respect to the quality of care, there were no associations found for do-not-resuscitate orders, foreseeable deaths and palliative treatment.

## Discussion

In 2012, there were 405 615 deaths in Spain according to official statistics, an increase of 4.6% on 2011. The crude death rate was 8.6 per thousand people. In our region there were 28 473 deaths, 5.2% more than the previous year, of which 4,808 occurred in the province of Valladolid[16].

Monitoring of hospital mortality helps to assess and improve the quality of care. Although data for 2012 have not been published, the 2011 survey of hospital morbidity reports 4 670 687 hospital discharges, of which 3.9% (183 410) were deaths[17].

Internal Medicine Services in Spain are characterized by the high mean age of the population attended, and a high prevalence of comorbidities, as reported by other studies of mortality in Internal Medicine Services, both international[9,18,19] and Spanish[3,12-14]. Zafrir et al[19] found a rate of hospital mortality of 22% in nonagenarian Israeli patients hospitalized in Internal Medicines Services in 2006, with the most common reason for admission being signs and symptoms of acute infection (82.4%). Older age, the degree of functional capacity, cognitive impairment and infections at admission, but not comorbidity or other factors, were associated with overall mortality. A nationwide study in Italy by Nobili et al[18] in 2008 found that overall mortality in Internal Medicine Services was 5%. The mean age of patients was 79.4 ± 7.5 years and 46% were aged > 80 years. Predictors of hospital mortality were age and comorbidity. In Spain, studies show differing mortality rates in Internal Medicine Services, ranging from the 4.7% found by Zambrana et al. [3] to the 9.5% found by Zapatero et al[12] in a recent study evaluating patients discharged from all Internal Medicine Services of Spanish National Health System hospitals, which also found that infectious diseases were the diagnostic category with the second-highest mortality (10.5%), including pneumonia, with a mortality rate approaching 7.5%, and urinary infections, with a mortality rate ranging between 1.7% and 15% depending on the presence of complications.

In our study, all-cause hospital mortality in the Internal Medicine service was 12.8%, and mortality due to infections was 5.8%, including the respiratory tract in 52.5% of cases (29% attributed to respiratory sepsis and 23.5% to severe pneumonia) followed by the urinary tract (16.6%). There are few comparable studies, al-

though Gómez et al. [5] found a rate of mortality due to infectious disease of 7.9% in Internal Medicine Services, while Martinez et al[20] found a rate of 9%, both somewhat higher than that shown by our results. Mortality attributed to pneumonia in our patients was higher than in other Spanish studies assessing overall mortality [13,14], but were similar to the rate found in studies of mortality specifically due to infections[21,22]. However, some studies, in contradiction to our results, have found that the most common source of infection was the urinary tract, followed by the respiratory tract[6,19,23].

Our study population had a female/male ratio of 1.1/1 and more than half the patients were aged > 85 years, factors consistent with the aging population characteristic of our health region, and thus confirming the representativeness of our sample.

A history of HT, DM, or cardiovascular, renal or lung disease in our series was higher than that described by other studies[6,23] as was comorbidity[22,23]. The higher rate of comorbidities found compared with other studies[12,22] is probably related to the older age of the cases included in our study. The CI was higher in patients aged < 85 years, possibly because patients with higher levels of comorbidity die at a younger age. We also found a greater prevalence of institutionalized and dependent patients, although the mean hospital stay was within the range found by other studies of 7.6-12 days[5,6].

Residency in a geriatric center, dependency for the activities of daily living, and cognitive impairment were associated with hospital mortality caused by infection in our study, as described by other studies[6,19], although no relationship with cerebrovascular disease with sequelae has previously been described. Contrary to our expectations, we found no relationship between deaths due to infections and age, CI, DM, hospital attendance, length of stay or admission in an end-of-life situation, unlike other studies[6,18,23].

There is little data on the quality of care of deaths[14]. As might be expected, most of our patients underwent palliative treatment and foreseeable mortality and do-not-resuscitate orders were included in the medical record. There is also little data on other clinical factors. Similar to other studies[6,22], only half our patients presented with fever at admission. Likewise, 16.5% presented with bacteremia with microbiological isolation in blood cultures. Various studies have emphasized the importance of appropriate antibiotic treatment and its relationship with mortality[6,20,23,24]. More than three-quarters of our patients received empirical antibiotic therapy, which was maintained because microbiological samples were collected in only half of the patients (which was somewhat higher than in other series[22]) and the yield was poor with respect to the detection of microorganisms.

An interesting, but little-reported, finding was that early death due to infection was three times higher than found in other studies[22].

A major limitation of our study is the retrospective design, as some data may be incomplete in digitized medical records. Likewise, our study was conducted in a single hospital, so that extrapolation of data to other hospitals and health areas should be made with caution.

## Conclusions

This study is the first qualitative and quantitative record of mortality due to infections in our health area and one of very few Spanish studies. Dementia, cerebrovascular disease, residence in a geriatric center and dependency were risk factors for in-hospital death due to infectious disease, but comorbidity, age and length of stay were not. The most-frequent cause of death was respiratory etiology. Further studies are necessary to enable us to improve the quality of care and better distribute health resources.

### Conflict of interest

All the authors state that they have no financial or other type of conflict of interest.

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