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Trends in sepsis incidence and outcomes among people with or without type 2 diabetes mellitus in Spain (2008–2012)

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ABSTRACT

Aims: There is conflicting evidence on how type 2 diabetes mellitus (T2DM) influences in-hospital mortality (IHM) in sepsis. We aimed to compare trends in outcomes for sepsis in people with or without T2DM in Spain between 2008 and 2012.

Methods: We identified all cases with any sepsis diagnosis using national hospital discharge data. We evaluated annual incidence rates for sepsis stratified by T2DM status. We calculated IHM and analyzed trends over time. In a multivariate analysis including potential confounding factors, we tested T2DM as an independent factor for IHM.

Results: Overall, 217,280 cases of any-stage sepsis were diagnosed, of whom 50,611 (23.3%) had T2DM. The annual incidence of sepsis increased during the 5-year period (from 76.5 to 113.3 cases/10^5 population). The incidence increase was higher for the population with T2DM (from 16.8 to 27.1 cases/10^5 population; 61.3% relative increment). People with T2DM were significantly older (75.8 ± 11.2 years vs. 71.0 ± 16.4 years) and suffered from more coexisting medical conditions. In the univariate analysis, mortality was higher for the population with T2DM only when septic shock was present (53.3% vs. 51.9%; $P = 0.002$). IHM decreased over time both in participants with (from 45.7% to 38.1%) and without T2DM (from 46.1% to 39.5%). After accounting for all other potential confounders, T2DM was significantly associated with a lower IHM (odds ratio = 0.88; 95% confidence interval, 0.86–0.90).

Conclusions: In Spain, the annual increase in sepsis incidence was higher in people with T2DM, but the risk of dying with sepsis during admission was moderately lower in people with T2DM.

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1. Introduction

We define sepsis as the systemic inflammatory response syndrome caused by an infection. Sepsis is severe when certain organs fail or if tissue hypoperfusion is present. Septic shock occurs if there is sepsis-induced hypotension despite adequate fluid resuscitation [1]. The incidence of sepsis may be increasing [2–4], but there may also be a greater sensitivity to diagnose sepsis in other cases that would otherwise have been coded as localized infections (i.e., pneumonia). Several authors have reported an association between diabetes and mortality in sepsis [5], whereas others support a neutral effect [6–8]. Explanations used to support any of these hypotheses are mostly speculative: on the one hand, a hampered immune cell function or a decreased bacterial clearance might pose a higher risk; on the other, a possible lower incidence of the acute respiratory distress syndrome or some antidiabetic drugs could confer protection against worse outcomes.

Diabetes is a prevalent chronic condition; thus, if we could add evidence that such a large population is differentially exposed to a higher mortality risk for sepsis, specific strategies should accordingly be designed to improve sepsis prognosis in people with diabetes. We thus aimed to compare trends in sepsis incidence rates and outcomes in people with or without type 2 diabetes mellitus (T2DM) in Spain for the period 2008–2012 using national hospital discharge data. In particular, we analyzed and compared participants' coexisting medical conditions and in-hospital outcomes, such as length of stay and in-hospital mortality for patients with sepsis between both groups. We focused on cases specifically codified as sepsis in all its different severity stages, as opposed to previous research work based on actively seeking codes of specific individual infectious diseases plus organ dysfunction [9–11].

2. Subjects, materials and methods

2.1. Subjects

We conducted this cohort-based, retrospective, observational study using the Spanish National Hospital Database (MBDS, Minimum Basic Data Set). This database is managed by the Spanish Ministry of Health, Social Policy and Equality and compiles all the public and private hospital data, hence covering more than 95% of hospital discharges [12]. The MBDS includes patient-related variables (sex, date of birth), date of admittance, date of discharge, up to 14 discharge diagnoses, and up to 20 procedures performed during the admission. The Spanish Ministry of Health, Social Policy and Equality sets standards for registration and performs periodic audits. We analyzed the available data, collected between January 1, 2008 and December 31, 2012 (5-year time period).

We chose disease criteria according to the International Classification Diseases-Ninth Revision, Clinical Modification (ICD-9-CM) [13], which is used in the Spanish MBDS. We selected all diagnostic admissions of cases with sepsis, severe sepsis and septic shock (ICD-9-MC codes, 995.91, 995.92 and 785.52, respectively), identified based on any diagnosis field. For this work, we decided to follow a restrictive definition of sepsis diagnoses using predefined sepsis codes as proposed by Lagu et al. [14], instead of more inclusive definitions [15]. We intended to achieve the highest diagnosis specificity as possible and thus provide actual estimations of the burden of the disease in the community.

We grouped discharge diabetes status as follows: people with no diabetes vs. people with T2DM. We identified T2DM with the ICD-9-CM codes: 250.x0 and 250.x2. We excluded people with type 1 diabetes mellitus (ICD-9-MC codes: 250.x1; 250.x3), people younger than 18 years old and the HIV positive population, whose response to infection might be different. Clinical characteristics included information on overall comorbidity at the time of diagnosis, which we assessed by computing the Charlson comorbidity index (CCI) [16,17]. The index applies to 17 disease categories whose scores are totaled to obtain an overall score for each case. The index is subsequently categorized into three levels: 0, no disease; 1, one or two diseases; and 2, three or more than three diseases. We used 15 disease categories after excluding diabetes and HIV infection to calculate our modified CCI.

We considered other risk factors in the data analysis: obesity, alcoholism, having been discharged home from a surgical service, and type and number of failing organs (for ICD-9-MC codes, see online-only supplemental Table S1). We also collected data on several procedures: mechanical ventilation, red cell transfusion, hemodialysis, vasopressor therapy, Swan-Ganz catheter, parenteral nutrition, tracheostomy and chest tube (online-only supplemental Table S1). The outcomes of interest included the proportion of participants who died during admission, defined as in-hospital mortality (IHM), and the length of hospital stay (LOHS). The nature of the database did not allow evaluate other outcomes, such as 30-day mortality.

2.2. Statistical analyses

We estimated sepsis incidence for the populations with and without T2DM per 100,000 inhabitants. We calculated the yearly age- and sex-specific incidence rates for people with T2DM and people without diabetes by dividing the number of cases by year, sex, and age group by the corresponding number of people in that population group according to data from the Spanish National Institute of Statistics, as reported at December 31 of each year [18]. We also determined the proportion of participants with T2DM hospitalized each year who presented a diagnosis of sepsis in any of its severity stages.

We obtained the values for the variables as proportions or rates, means with standard deviations or medians with interquartile ranges (LOHS). We conducted bivariate analyses of the variables according to the year using binary logistic regression (proportions), ANOVA (means) and Kruskall–Wallis test (medians) as appropriate. In order to test the time trend for IHM adjusted by potential confounding variables, we performed logistic regression analyses with mortality as a binary outcome, including year of discharge, sex, age, CCI, discharge from surgical services and obesity as independent variables in the model. We generated models for subjects with and without T2DM and for the entire population in order to