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# The clinical epidemiology and malignancies associated with *Streptococcus bovis* biotypes in 506 cases of bloodstream infections<sup>☆</sup>

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## KEYWORDS

*Streptococcus bovis*;  
 Biotypes;  
 Bacteraemia;  
 Endocarditis;  
 Mortality;  
 Colorectal neoplasm;  
 Malignancies;  
 Colonoscopy;  
 Cattle area;

**Summary Objectives:** To determine the incidence of *Streptococcus bovis* (Sb) biotypes causing bacteraemia and associated malignancies.

**Methods:** This is a retrospective analysis of patients with Sb bacteraemia, pulled out from a prospective surveillance protocol of bacteraemia cases, in three areas of Spain (1990–2013): a cattle area (Lugo), a fishing area (Ferrol) and an urban area (Barcelona). Colonoscopy and Sb biotypes (Sb-I and Sb-II) were determined in most cases.

**Results:** 506 patients with Sb bacteraemia; mean age 68.1 (±14.1) years, and 66.2% were males. The cattle area, compared with the fishing and urban areas, had higher incidence of bacteraemia by Sb-I (40.29 vs 9.38 vs 6.15 cases/10<sup>6</sup> person-years, P < 0.001) and bacteraemia by Sb-II (29.07 vs 9.84 vs 13.37 cases/10<sup>6</sup> person-years, P < 0.001).

<sup>☆</sup> This manuscript has not been presented at a meeting.

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Rural area;  
Urban area;  
Fishing area

The Sb-I cases (N = 224), compared with Sb-II cases (n = 270), had greater rates of endocarditis (77.6% vs 9.6%,  $P < 0.001$ ) and colorectal neoplasm (CRN) (50.9% vs 16.6%,  $P < 0.001$ ), and smaller rates of biliary tract infection (2.2% vs 29.6%,  $P < 0.001$ ) and non-colorectal malignancy (8.9% vs 31.4%,  $P < 0.001$ ).

**Conclusion:** There was a link between the cattle area and higher incidence of Sb bacteraemia. Sb-I differed from Sb-II cases in clinical findings and associated malignancies. Colonoscopy is mandatory in cases of endocarditis or bacteraemia caused by Sb-I.

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## Introduction

*Streptococcus bovis* (Sb), previously included in group D streptococci, is a group of bacteria that colonize the gut of animals and human beings. Several reports have found an association of Sb with endocarditis and colorectal neoplasm (CRN), in particular with biotype I (Sb-I) – called *Streptococcus gallolyticus* subspecies *gallolyticus*.<sup>1–4</sup> Also, it has been suggested that biotype II (Sb-II), which includes *Streptococcus infantarius* (Sb-II.1) and *S. gallolyticus* subspecies *pasteurianus* (Sb-II.2), is less often associated with endocarditis, but is frequently associated with other types of infections and non-CRN.<sup>1,2,4–7</sup> However, it should be noted that most published studies of Sb bacteraemia did not perform Sb biotypes or were short reports with discordant results.

Some reports have shown geographical differences in the Sb bacteraemia, including incidence rate, source of infection and association with CRN. For example, Sb endocarditis is more common in Europe than in the United States,<sup>8</sup> and within Europe there are differences between the North and South.<sup>9</sup> In addition, reported data suggest that in Europe, North America and Australia Sb endocarditis and CRN predominate,<sup>1,2,4,10</sup> while in Asia Sb hepatobiliary infection predominates.<sup>5,6</sup>

It has been suggested that bacteraemia and endocarditis caused by Sb are increasing in certain geographic areas,<sup>3,11–13</sup> and that some of these infections may be linked to rural setting.<sup>13,14</sup> Some factors such as diet or animal contact might have a role in human intestinal colonization by Sb.<sup>14,15</sup> A previous study of our group has also suggested an increased rate of Sb endocarditis in rural setting,<sup>16</sup> being higher than those reported in other hospitals of our country.<sup>17–19</sup>

We studied a large cohort of patients with Sb bacteraemia including the following issues: 1) Incidence of Sb bacteraemia in three geographical areas; 2) Comparison of clinical findings between Sb-I and Sb-II cases; and 3) The association of Sb-I and Sb-II with malignancies.

## Methods

This is a retrospective observational study of Sb bacteraemia in adult patients who were admitted to three hospitals in Spain from 1/1990 to 12/2013. Hospital Lugo (HL) and Hospital Ferrol (HF), both located in Galicia county in the northwest of Spain (Atlantic region), and Hospital Bellvitge (HB) located in Barcelona, Catalanian county in the northeast of Spain (Mediterranean region). The Hospital Lugo is a teaching hospital with 690-beds

servicing an area of approximately 230.000 inhabitants, which is mainly a cattle production area. The Hospital Ferrol is a teaching hospital with 350-beds serving an area of approximately 210.000 inhabitants, which is mostly a fishing area; both institutions have no cardiac surgery or organ transplantation programs. The Hospital Bellvitge is a 900-bed university hospital, which serves an overall population of about one million people in an urban area, and it has an active program of organ transplantation and cardiac surgery. All three institutions have a prospective surveillance protocol of all patients with bacteraemia. The present study is based on a retrospective analysis of patients with Sb bacteraemia, pulled out from that prospective surveillance protocol of bacteraemia cases. Overall, there were 509 episodes of Sb bacteraemia, 506 of them were included in the study and the other three aged <18 years were excluded.

## Characteristics of the three geographical areas

The Hospital Lugo gives medical care mainly to a rural population, which is an important cattle production area, being one of the first producers of meat and milk in Spain, and the vast majority of the population is cattleman; they eat mainly beef and pork with a low intake of vegetables.<sup>20,21</sup> The Hospital Ferrol is located in the Atlantic coast, serving a large fishing and shipping population area; their diet differs from that of the cattle production area in a higher intake of fish and less often meat.<sup>20,21</sup> The Hospital Bellvitge is located in Barcelona and serves an urban population; the diet is mainly a “Mediterranean diet”, which is rich in vegetables and with less intake of beef and pork.<sup>20,22</sup>

## Definitions

Clinically significant bacteraemia was defined according to Weinstein criteria<sup>23</sup> and the diagnosis of endocarditis was based on modified Duke’s criteria.<sup>24</sup> Hospital-acquired bacteraemia was considered when a patient develops signs or symptoms of infection after 48 h of admission. We considered an immunocompromised patient when he/she had a prior diagnosis of an immunosuppressive condition including HIV infection, splenectomy, solid organ/haematologic transplant or received immunosuppressive therapy. Diagnosis of liver cirrhosis was based upon clinical and laboratory criteria with or without liver biopsy. The severity of the underlying disease was estimated by the McCabe Jackson score.<sup>25</sup> Mortality was considered as death occurred within 30 days after the diagnosis of bacteraemia.

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