



Correlation between *Streptococcus bovis* bacteremia and density of cows in Galicia, northwest of Spain

J. Corredoira¹ · E. Miguez² · L. M. Mateo³ · R. Fernández-Rodríguez⁴ · J. F. García-Rodríguez⁵ · A. Pérez-González⁶ · A. Sanjurjo⁷ · M. V. Pulian⁸ · R. Rabuñal¹ · GESBOGA

Received: 8 September 2018 / Accepted: 15 November 2018 / Published online: 29 November 2018
© Springer-Verlag GmbH Germany, part of Springer Nature 2018

Abstract

Background There are few data on the epidemiology of infections caused by *Streptococcus bovis* (Sb). Some studies suggest that both residence in rural areas and contact with livestock could be potential risk factors.

Methods We performed a retrospective study for the period 2005–2016 of all cases of bacteremia caused by Sb in Galicia (a region in the northwest of Spain). The association between the incidence rate of Sb bacteremia and the number of cattle by province and district was analyzed.

Results 677 cases were included with a median age of 76 years, 69.3% males. The most frequent infections were endocarditis (234 cases, 34.5%), primary bacteremia (213 cases, 31.5%) and biliary infection (119 cases, 17.5%). In 252 patients, colon neoplasms were detected (37.2%). *S. gallolyticus* subsp. *gallolyticus* was the predominant species (52.3%). Mortality was 15.5% (105 cases). The annual incidence rate was 20.2 cases/10⁶ inhabitants and was correlated with the density of cattle ($p < 0.001$), but not with rurality. When comparing the two provinces with a strong predominance of rural population, but with important differences in the number of cattle, such as Orense and Lugo, with 6% and 47.7% of Galician cattle, respectively, the rates were very different: 15.8 and 43.6 cases/10⁶, respectively, with an RR of 2.7 (95% CI, 2.08–3.71). Some districts of the province of Lugo had rates higher than 100 cases/10⁶ inhabitants.

Conclusions Our study shows a significant correlation between the rates of Sb bacteremia and cattle density, suggesting a possible transmission of Sb from cows to people.

Keywords *Streptococcus bovis* · Bacteremia · Cattle

Introduction

Streptococcus bovis and *Streptococcus equinus* were described a century ago as the predominant streptococci in the intestine of cows and horses [1]. Since then, several species and subspecies have been described within this group, currently called *Streptococcus bovis*/*Streptococcus equinus* complex (SBEC) and there have been numerous changes in its taxonomy and nomenclature that have been recently revised [2].

Currently, the clinical associations of the different species within this complex are well known. *S. gallolyticus* subsp. *gallolyticus* or *S. bovis* biotype I (*S. gallolyticus*) is mainly associated with endocarditis and colon neoplasms [3, 4]. The two species formerly classified as biotype II, now called *S. gallolyticus* subsp. *pasteurianus* (*S. pasteurianus*) and *S. infantarius*, have been associated with infections of the biliary tract, urinary tract, meningitis, neonatal sepsis, liver disease and non-colorectal cancer [5–9]. On the other hand, recent studies suggest not only a clinical association of *S. gallolyticus* with colorectal cancer, but a possible etiological role in it [10, 11].

Unlike the clinic, the epidemiology of these infections is poorly understood. There are important geographical disparities in their incidence and types of infection [3, 5, 12], although their causes are unknown. Some studies suggest that rural populations would have a higher incidence than urban populations [13–15]. The proportion of endocarditis

The list of participating centers and researches in GESBOGA—Study Group of *Streptococcus bovis* bacteremia in Galicia—has been provided in Acknowledgements.

✉ R. Rabuñal
ramon.rabunal.rey@sergas.es

Extended author information available on the last page of the article

and the incidence of bacteremia caused by SBEC are higher in France and in some areas of Spain [16, 17]. The incidence of bacteremia by SBEC is approximately four times higher in Lugo (rural area) than in Barcelona (urban area) [17]. While in the whole of Spain endocarditis caused by SBEC accounts for 6.5% of the total [18], in the Lugo area they represent 25% [19].

SBEC causes diseases in wild animals, farm animals and pets. Some of these diseases are similar to those produced in humans, which could indicate a possible zoonotic origin [20, 21]. A close contact with animals or the consumption of their products could be the source of human infection, as has been demonstrated in other streptococci, such as *S. suis* or *S. equi* subsp. *zooepidemicus* [22, 23]. Given that members of the SBEC are isolated in almost 100% of the cattle in their rumen [24], we have postulated in a previous work [17] that the high rate of cases of SBEC bacteremia in our area could be due to the high density of cattle in our environment.

The objective of this research is to study bacteremia by SBEC in our geographical area to analyze in a well-defined population the possible differences in the incidence of bacteremia by SBEC during a defined period (2005–2016), and if these differences can be related to rural habitat and contact with the cattle.

Methods

Social and geographic scope

Galicia is an autonomous community located in the north-west of Spain, in southern Europe (Fig. 1). It has an area of 29,574 km², and at the midpoint of the study period (year

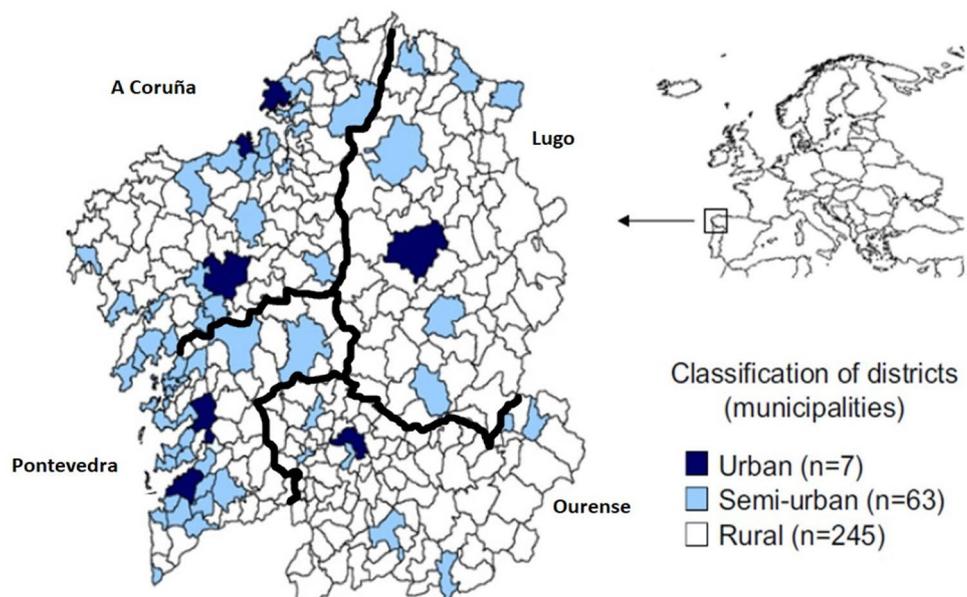
2010) it had 2,772,457 inhabitants. Administratively, it is divided into 4 provinces, 53 districts and 315 municipalities (Figs. 1, 2). The population is unequally distributed. One-third of the population lives in an urban environment, and the rest lives in rural or semi-urban areas. The two Atlantic provinces, Pontevedra and A Coruña, are the most populated, with a predominantly urban population and concentrated along the coast. The two provinces of the interior, Ourense and Lugo, have a lower population density, which lives mostly dispersed in rural areas, with greater dedication to agriculture and livestock and with a high percentage of the elderly population (Table 1). Galicia is one of the communities with the highest rurality index in Spain [25]. Of the 315 municipalities, only 7 are urban (Fig. 1).

Galicia, with 2,407,000 tons per year, is the leading autonomous community producing milk in Spain [26] and the second largest producer of cattle, with a census of 963,368 cattle in 2010 (Table 2). The farms are small, 50.3% of the more than 45,000 census farms have less than ten animals [27] and their geographic distribution is irregular, with predominance in the central zone of the province of Lugo (Fig. 2a). Since the land ownership regime is a smallholding, contact between animals and humans has traditionally been very close, with the animals living very close to the houses.

Definition of cases

More than 99.6% of our population is covered by the National Health System, which in Galicia has 15 public hospitals. Eleven microbiology services provide coverage to these centers, with which we contacted to collect all blood cultures positive for SBEC isolated between January 2005 and December 2016. The blood cultures were processed

Fig. 1 Map of Galicia, showing the division into urban, semi-urban and rural areas



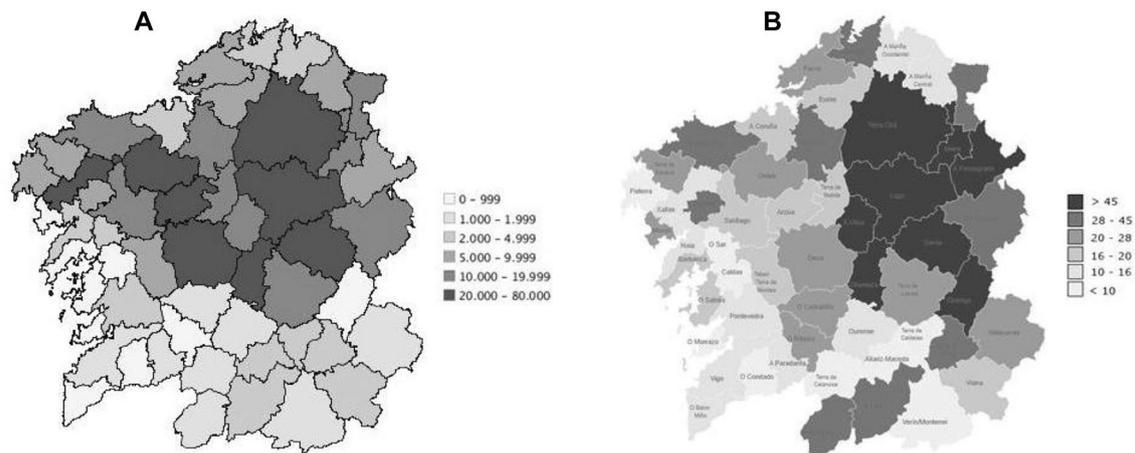


Fig. 2 Distribution by districts of the density of cattle (a) and of the rate per million inhabitants of bacteremia by *Streptococcus bovis* (b)

Table 1 Population characteristics of the Galician provinces

Characteristics	Orense	Lugo	A Coruña	Pontevedra
Population (2010)	331,649	351,000	1,138,107	951,701
Population > 64 years	29%	28%	21%	19%
% of rural or semi-urban municipalities	93%	88%	69%	54%
% of farmers	4.8%	9.6%	3.1%	1.7%

according to the standard criteria applied to all the participating microbiology laboratories.

The clinical histories of all patients were retrospectively reviewed, collecting clinical, epidemiological and microbiological data. The definition of bacteremia and endocarditis was made according to previously published criteria [17]. All the protocols were reviewed and validated by two investigators not involved in the care of the corresponding case.

The incidence rate was calculated, expressed as the number of cases/ 10^6 inhabitants, dividing the number of episodes recorded within the study years by the population of each district at the midpoint of the study period (year 2010). An ecological study was also carried out using each district

as a unit of study. The municipalities of each district were grouped into three subgroups depending on the rurality index of each one. Data of the population census and number of head of cattle grouped by provinces and by district were extracted from the Web page of the Galician Institute of Statistics (<http://www.ige.es>) [27]. To classify the areas as rural, semi-urban or urban, the classification of the rurality index established by the Galician autonomous government was used [25].

Statistical analysis

The quantitative variables were expressed as mean \pm SD. The qualitative variables were expressed as absolute number and its percentage. We calculated case rates, both global and by different socio-demographic groups (such as province, sex, age) and relative risks were computed. The association between the rate of SBEC bacteremia cases per district and the number of bovines was analyzed using the Spearman correlation test.

A regression of generalized additive models (GAM) with a Poisson response was performed to determine the association between the number of cases and different

Table 2 Livestock, in numbers, in Galicia by provinces

Year 2009	Avian	Porcine	Ovine	Equine	Bovine	Bovine/human relationship
A Coruña	1,386,500	305,011	30,535	6026	344,003	0.30
Lugo	3,580,000	225,777	57,149	8414	454,483	1.29
Orense	5,654,428	399,745	74,191	2931	61,200	0.18
Pontevedra	4,082,071	223,870	24,175	2689	112,554	0.10
Total	14,703,000	1,154,403	186,050	20,060	963,316	0.34

socio-demographic factors. The number of cattle, the rate of inhabitants over 65, the rate of men, the province of origin and the rurality were introduced as explanatory variables in the model. It was adjusted for the size of the population by incorporating the logarithm of the number of inhabitants as an offset term for the GAM model.

All analyses were performed with the statistical software IBM SPSS Statistics 19.0 and R 3.3.2.

Table 3 Types of infection and underlying diseases associated with *Streptococcus bovis* bacteremia

	Number of cases (%)
<i>Type of infection</i>	
Endocarditis	234 (34.5%)
Primary bacteremia	213 (31.5%)
Biliary infection	119 (17.5%)
Abdominal	44 (6.5%)
Urinary	27 (4%)
Others	40 (5.9%)
<i>Underlying diseases</i>	
Diabetes mellitus	166 (24.5%)
Non-colorectal cancer	154 (22.7%)
Colorectal neoplasia ^a	252 (37.2%)
Cirrhosis	54 (7.9%)
Chronic renal failure	53 (7.8%)
Immunosuppression	52 (7.6%)
	Mean ± SD
Charlson comorbidity index	2.7 ± 2.1
Age-adjusted Charlson comorbidity index	5.6 ± 2.6

^aIncludes adenomas and carcinomas

Table 4 Isolates of *S. bovis* by year of study

Year	<i>S. gallolyticus</i> subsp. <i>gallolyticus</i>	<i>S. infantarius</i>	<i>S. gallolyticus</i> subsp. <i>pasteurianus</i>	Others ^a	<i>S. bovis</i> group	Total
2005	9	6	3	2	16	36
2006	16	2	1	1	26	46
2007	9	2	1	1	23	36
2008	11	5	2	2	18	38
2009	6	2	4	1	30	43
2010	5	4	3	3	31	46
2011	19	4	9	2	28	62
2012	14	27	2	0	27	70
2013	28	14	6	2	20	70
2014	45	8	14	3	11	81
2015	35	17	18	1	7	78
2016	30	19	14	2	6	71
Total	227	110	77	20	243	677

^a*S. equinus* (5), *S. alactolyticus* (1) and *S. bovis* biotype II (14)

Results

Basic demographic data

During the study period, 677 episodes were detected with positive blood cultures for SBEC. There were 11 reinfections, occurring between 5 and 53 months after the first episode, and 5 recurrences. The median age was 76 ± 13.3 years, and 69.3% were males. Only four cases were pediatric (0.6%). Hospital admissions did not follow a seasonal distribution, and the annual distribution ranged from 36 cases in 2005 to 81 in 2014, with a progressive increase throughout the study, from 156 cases in the first 4 years to almost double in the last 4 years (300 cases).

Clinical and microbiological data

The most frequent types of infection and the main underlying diseases are reflected in Tables 3 and 4. Colonoscopy was performed in 418 patients (61.7%), with neoplasms found in 60.2% (252 cases).

In 119 cases (17.5%), SBEC was isolated in a single blood culture and in the rest in two or more, all considered clinically significant. Identification at the species level improved throughout the study period, so that during the first 4 years of the study it was only carried out in 46.8% of the isolates (73/156), while in the last 4 years, it was performed in 85.3% (256/300). *S. gallolyticus* subsp. *gallolyticus* was the predominant species, with 52.3% of cases. 24.2% of bacteremias (164) were polymicrobial, with *E. coli* being the most frequent microorganism, with 76.2% of these cases (Table 4).

Geographic distribution of cases

Only 2 cases were from outside the community. The distribution of cases according to the place of residence followed a distribution similar to that of the Galician population, with 226 cases being urban (33.4%) and rural or semi-urban: 449 cases (66.6%), with a rate of 18.8 and 20.8 cases/10⁶ inhabitants, respectively ($p = 0.219$). The overall rate was 20.2 cases/10⁶ inhabitants, and in patients older and younger than 14 years, it was 22.8 and 1.0 cases/10⁶ inhabitants, respectively ($p < 0.001$). The rate among men was 28.9 cases/10⁶ inhabitants, while among women it was 11.5 cases/10⁶ inhabitants ($p < 0.001$).

In terms of spatial distribution, significant differences were obtained in the case rate by province ($p < 0.001$),

Table 5 Bacteremia by *Streptococcus bovis*

Comparison	RR	<i>p</i>
Lugo–A Coruña	2.12 (1.76–2.55)	<0.001
Lugo–Ourense	2.76 (2.08–3.71)	<0.001
Lugo–Pontevedra	3.39 (2.73–4.22)	<0.001
A Coruña–Ourense	1.30 (1.01–1.72)	0.056
A Coruña–Pontevedra	1.60 (1.31–1.96)	<0.001
Pontevedra–Ourense	0.81 (0.61–1.10)	0.183

Rates for 10⁶ inhabitants and relative risks by province

RR relative risks of the first province with respect to the second

with Lugo (almost 50% of Galician cattle) being the province with the highest relative risk compared to the other three (Table 5). Coruña also has a greater risk over Ourense and Pontevedra. The eight districts with the highest rate of cases were from the province of Lugo, ranging from 46.3 to 109 cases/10⁶ inhabitants, in the Fonsagrada district. This district had a ratio between cattle/humans of 2.8, surpassed only by the district of Meira (ratio 3.1). Of the five districts with the lowest case rates, four were from the province of Ourense (only 6% of Galician cattle), ranging from 0 to 5.6 cases/10⁶ inhabitants. The distribution of cases by districts is shown in Fig. 2.

Regarding the ecological study, the association of the different socio-demographic factors with the ratio of the number of cases using a GAM regression model is represented in Fig. 3. The association between the number of cattle and the number of cases has a positive tendency ($p < 0.001$). The association with the male rate is not significant ($p = 0.186$), while with the rate of over 65 years, it does not have a clear effect, although it presents a positive trend. No significant differences were observed between the rural and non-rural areas ($p = 0.175$), and among the provinces, Lugo was obtained as a significant risk factor ($p = 0.002$).

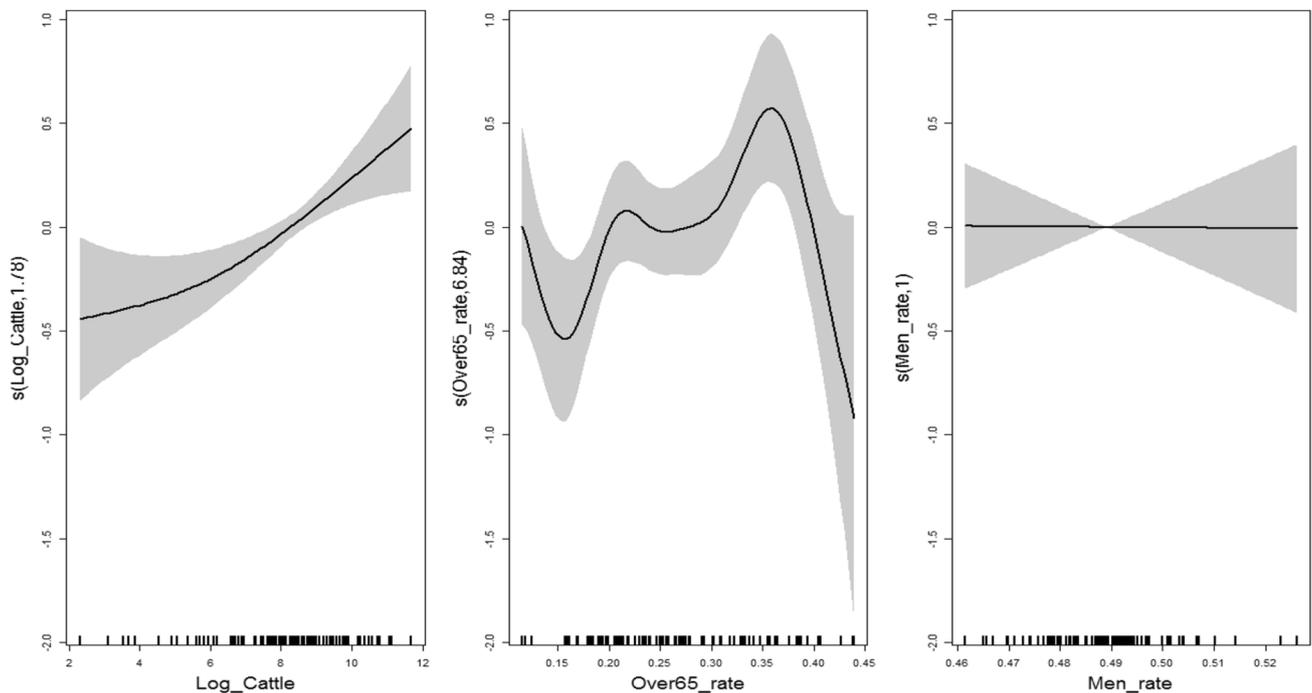


Fig. 3 Estimated associations (95% CI) between the number of cases and socio-demographic factors

Discussion

There are few multicenter studies on bacteremia by SBEC. A limitation of them is that they provide few cases or include few centers, they are not population studies, they analyze mainly urban populations or they are limited to a partial aspect of bacteremia, such as endocarditis [9, 16, 17, 28, 29].

The strength of our study is that it analyzes a wide series of cases, compiled from many hospitals of different health levels that include a well-defined population, with a strong rural predominance, and that covers almost 100% of the population. Furthermore, it contemplates all types of bacteremia caused by SBEC, not just endocarditis. This allows us to exclude possible biases and give us a broad view of the clinical spectrum and the epidemiology of the disease.

Our patients are of more advanced age, and with a lower percentage of pediatric cases than in other studies [3, 5–7]. As in other previous studies [15, 17], the number of cases has progressively increased throughout the study period. We do not know the reasons, but the increase in the average age of the population (it increased in 2 years throughout the study) and, on the other hand, a greater awareness on the part of the microbiology laboratories in the correct identification of streptococci isolated in blood cultures may have contributed to this. Within the SBEC, *S. gallolyticus* was the predominant species, doubling and tripling the number of *S. infantarius* and *S. pasteurianus*, respectively. Due to this, endocarditis and colon neoplasms were the most frequent clinical associations [30]. In other studies, in which the predominant species is *S. pasteurianus*, the underlying infection and pathology types are markedly different [5–7].

We found a significant correlation between the density of cattle and the incidence of SBEC bacteremia cases. The rates were much higher in Lugo than the rest of Galicia. When we compared the provinces of Ourense and Lugo, both with a predominance of rural population and a high proportion of the elderly, the differences in bacteremia rates were marked: 15.8 vs. 43.6 cases/10⁶, respectively. Lugo has 47.7% of Galician cattle and Ourense 6%, although the latter is nevertheless the Galician leader in sheep, pigs and poultry.

Our rates are difficult to compare with other studies in our country, given that there are no population studies [9, 28, 31]. In a multicenter study conducted in Andalusia, which includes a period of 9 years and seven hospitals with a high reference population, the number of cases was 92, much lower than our 677 [28]. However, in a French population study on endocarditis [13], the rate per 10⁶ in adults ranged from 11.6 in Ile de France, an urban area, and 26.8 in Marne, a rural area. These figures are higher than the Galician average, which was 7.7, but somewhat lower than the rate of the central Lugo area, which was 28.3, and it includes 78% of the cattle of the province [27].

We do not know the reason for these differences, but a recent study analyzed the risk factors of intestinal colonization by *S. gallolyticus* in humans [32]. It showed a significant association with close contact with animals and the use of manure as fertilizer, but not with rural residence. Although the route of SBEC transmission and its potential zoonotic potential is unknown, a case of a farmer has recently been published, with an endocarditis caused by *S. gallolyticus*, in which the same clone has been isolated in the chickens of his farm [20]. These authors explain the possible mechanisms of transmission between animals, and from animals to man, through contaminated surfaces, dust and inhalation or ingestion of bioaerosols [20]. These findings could suggest that in rural areas with high density of cattle, such as Lugo and some areas of France, which are among the maximum producers of beef and milk from Spain and the European Union, respectively [26, 33], there could be a transmission of animals to humans, which would justify these higher rates of SBEC infection. In addition to cattle density, the cattle/human ratio may be important, which in eight Galician districts (7 of them in Lugo) oscillate between 2.2 and 3.1. This percentage is close to that of Uruguay, one of the world leaders in the number of bovines, and within them, the first in the relationship between cattle and inhabitants, which is 3.2 [33].

Another fact that could support our hypothesis is the high incidence in the province of Lugo of tuberculosis caused by *Mycobacterium bovis*. This zoonosis is transmitted to humans mainly by cattle or by the ingestion of their products. While in the rest of Galicia, *M. bovis* was the cause of 0.64% of tuberculosis, with a rate of 2.1/10⁶, in Lugo it caused 4.7%, with a rate of 9.5/10⁶ (8 and 4.5 times higher, respectively) [34]. Taken together, all these data suggest a causal relationship of cattle density with infections caused by *Mycobacterium bovis* and *Streptococcus bovis*.

Of the three species of SBEC that usually produce infections in humans, *S. gallolyticus* was the predominant species in our study, and *S. pasteurianus* the least frequent. In other studies conducted in other European countries in which there is a significant amount of cattle, also *S. gallolyticus* was the species that was isolated more frequently [12, 13, 35]. It is probable that in these areas and in ours, this type of animals are the main reservoir of *S. gallolyticus*, since it is capable of metabolizing a wide range of complex carbohydrates and of detoxifying toxic substances that are found in the rumen of cattle. The comparative study of the genome of *S. gallolyticus* with *S. pasteurianus* and other members of the SBEC shows that the latter have lost pathogenicity mechanisms and would be less adapted to the intestine of ruminants [36–39]. In geographical areas with a low amount of cattle, such as some countries of East Asia, *S. pasteurianus* produce the

majority of the bacteremia caused by SBEC [5–7], so the reservoir and transmission mechanisms are probably different from those found in some European countries.

Although we have found a strong correlation between the rate of bacteremia by SBEC and cattle, our data have to be interpreted with caution since our study has several limitations:

First of all, it is an ecological design study. These studies are very interesting, but they are very exposed to biases, called “ecological fallacy”. In general, they serve to generate hypotheses, but we must be very cautious with the conclusions obtained from them, although given the close relationship of the SBEG with ruminants in general and with cattle in particular, our hypothesis seems totally plausible.

Secondly, it is a retrospective study, so it was not possible to analyze possible individual risk factors, such as contact with livestock, as a possible means of transmission. However, in certain areas of Galicia, contact with cattle is very common among the rural population.

Third, we have only examined the possible relationship of the infections caused by the SBEC group with cattle, but not with other types of animals or food. In a study conducted on farms in Germany, 91% of turkeys were colonized by *S. gallolyticus* [40], so transmission to humans could also be through birds. On the other hand, other members of the SBEC group such as *S. macedonicus* have been isolated in some varieties of Greek cheese [41] and in other types of cheese from southern European countries. In addition, different members of the *S. infantarius* group have been isolated in fermented foods, such as dairy products, cereals or fish in several areas of Africa, Mexico, Bangladesh or Thailand [21, 42]. These foods could be a hypothetical transmission mechanism.

Fourth, the methods of microbiological identification were not the same in all the hospitals, and in the same hospital they varied over the years. Although in the last years of the study period, most of the SBEC isolates were identified at the species and subspecies level in almost all the participating hospitals, during the first years this was not very frequent. The recent introduction of MALDI-TOF in Galician hospitals may have contributed to this. It is very important that the microbiology laboratories, both medical and veterinary, as well as food control, correctly identify the members of the SBEC, differentiating the different species and subspecies according to the current taxonomy [31, 43], to determine with greater precision if there are differences in the epidemiology between the species that make up the SBEC. This also has important health implications: on the one hand, they can help us diagnose very serious diseases, such as endocarditis or intestinal cancer [4, 30] and, on the other, know the biosecurity of foods, given that there are bacteria involved in their fermentation and are consumed by millions of people in the world [21, 39]. They also produce

diseases in livestock that cause significant economic losses [21].

Finally, to confirm our hypothesis, studies of the intestinal microbiota of animals and humans are necessary to establish whether they share the same species and the same clones. The MSLT (multilocus sequence type) could be a powerful tool to investigate the transmission of zoonotic pathogens [44]. Previous studies suggest that there are specific clones of animals and humans and others shared by both and could explain the possible mechanisms of transmission between animals and from animals to man [21].

In conclusion, our study demonstrates important differences in the incidence rates of SBEC bacteremia cases among predominantly rural population areas, and for the first time, plausibly suggests a relation of these with the density of cattle. More studies are needed to confirm this apparent zoonotic potential of SBEC.

Acknowledgements List of Collaborators: GESBOGA—Study Group of *Streptococcus bovis* bacteremia in Galicia: List of participating centers and researches: Hospital da Costa (Burela, Lugo): Serrano M (Microbiology), Jove MJ (Internal Medicine); Hospital Comarcal de Monforte de Lemos (Lugo): Alonso P (Microbiology), Justo E, Piñeiro JC (Internal Medicine); Hospital Universitario Lucus Augusti (Lugo): Alonso MP, García-Garrote F, Coira MA (Microbiology), Blanco A (Methodology and Clinical Research Unit. Ramón Domínguez Foundation), Gómez-Méndez R (Internal Medicine), García-Pais MJ, Rabuñal R, López-Álvarez MJ, J Corredoira, Eva Romay (Infectious Diseases Unit); Hospital Virxe da Xunqueira (Cee, A Coruña): Abel V (Internal Medicine); Complexo Hospitalario Universitario A Coruña (A Coruña): Míguez E (Infectious Diseases Unit), Cerezales A, Vieito D (Internal Medicine), Rodríguez-Mayo M, Gude MJ (Microbiology); Complexo Hospitalario Universitario de Ferrol (Ferrol, A Coruña): García-Rodríguez JF (Infectious Diseases Unit), Agulla JA (Microbiology); Complexo Hospitalario Universitario de Santiago (Santiago de Compostela, A Coruña): Mateo LM, González-Quintela A (Internal Medicine), Hernández M, Manso T, Aguilera A, Pérez del Molino ML (Microbiology), Hospital da Barbanza (Ribeira, A Coruña): Martínez-Braña L (Internal Medicine); Complexo Hospitalario Universitario de Ourense (Ourense): Fernández-Rodríguez R (Infectious Diseases Unit), Paz MI (Microbiology); Hospital de Valdeorras (O Barco de Valdeorras, Ourense), González-Domínguez M (Microbiology), Morales F (Internal Medicine); Hospital de Verín (Verín, Ourense): Soto I (Internal Medicine); Complexo Hospitalario Universitario de Vigo (Vigo, Pontevedra): Vasallo FJ (Microbiology), Pérez-Gonzalez A, Pérez-Alvarez R (Internal Medicine); Hospital POVISA (Vigo, Pontevedra): de la Fuente J, Sanjurjo A, Lamas JL, Álvarez-Ferreiro J (Internal Medicine), Rodríguez-Conde MI (Microbiology), Hospital do Salnes (Vilagarcía de Arousa, Pontevedra), Pazos A (Internal Medicine); Complexo Hospitalario Universitario de Pontevedra (Pontevedra), Pulian MV, Guzmán DM, García-Campello M (Microbiology), Diz J (Internal Medicine).

Funding No grant support was available for this investigation.

Compliance with ethical standards

Ethical statement The Institutional Review Boards approved this study, and they specifically waived the need for consent because the

study analyzed the data retrospectively and the source of data was anonymized.

Conflict of interest All authors declare no conflicts of interest with this investigation.

References

- Corredoira J, Rabuñal R, Alonso MP. *Streptococcus bovis*: 100 years of an intriguing pathogen. *Clin Microbiol Newslett*. 2017;39:1–9.
- Dekker JP, Lau AF. An update on the *Streptococcus bovis* group: classification, identification, and disease associations. *J Clin Microbiol*. 2016;54:1694–9.
- Ruoff K, Miller SI, Garner CV, Ferraro MJ, Calderwood SB. Bacteremia with *Streptococcus bovis* and *Streptococcus salivarius*: clinical correlates of more accurate identification of isolates. *J Clin Microbiol*. 1989;27:305–8.
- Boleij A, van Gelder MM, Swinkels DW, Tjalsma H. Clinical importance of *Streptococcus gallolyticus* infection among colorectal cancer patients: systematic review and meta-analysis. *Clin Infect Dis*. 2011;53:870–8.
- Lee RA, Woo PC, To AP, Lau SK, Wong SS, Yuen KY. Geographical difference of disease association in *Streptococcus bovis* bacteraemia. *J Med Microbiol*. 2003;52:903–8.
- Jean S, Teng LJ, Hsueh PR, Ho SW, Luh KT. Bacteremic *Streptococcus bovis* infections at a university hospital, 1992–2001. *J Formos Med Assoc*. 2004;103:118–23.
- Sheng WH, Chuang YC, Teng LJ, Hsueh PR. Bacteraemia due to *Streptococcus gallolyticus* subspecies *pasteurianus* is associated with digestive tract malignancies and resistance to macrolides and clindamycin. *J Infect*. 2014;69:145–53.
- Matesanz M, Rubal D, Iñiguez I, Rabuñal R, García-Garrote F, Coira A, et al. Is *Streptococcus bovis* a urinary pathogen? *Eur J Clin Microbiol Infect Dis*. 2015;34:719–25.
- Gómez-Garcés JL, Gil Y, Burillo A, Wilhelmi I, Palomo M. Diseases associated with bloodstream infections caused by the new species included in the old *Streptococcus bovis* group. *Enferm Infecc Microbiol Clin*. 2012;30:175–9.
- Corredoira J, Grau I, García-Rodríguez JF, García-País MJ, Rabuñal R, Ardanuy C, et al. Colorectal neoplasm in cases of *Clostridium septicum* and *Streptococcus gallolyticus* subsp. *gallolyticus* bacteraemia. *Eur J Intern Med*. 2017;41:68–73.
- Kumar R, Herold JL, Schady D, Davis J, Kopetz S, Martinez-Moczygemba M, et al. *Streptococcus gallolyticus* subsp. *gallolyticus* promotes colorectal tumor development. *PLoS Pathog*. 2017;13:e1006440.
- Beck M, Frodl R, Funke G. Comprehensive study of strains previously designated *Streptococcus bovis* consecutively isolated from human blood cultures and emended description of *Streptococcus gallolyticus* and *Streptococcus infantarius* subsp. *coli*. *J Clin Microbiol*. 2008;46:2966–72.
- Giannitsioti E, Chirouze C, Bouvet A, Béguinot I, Delahaye F, Mainardi JL, et al. Characteristics and regional variations of group D streptococcal endocarditis in France. *Clin Microbiol Infect*. 2007;13:770–6.
- Corredoira J, Alonso MP, Pita J, Alonso-Mesonero D. Association between rural residency, group D streptococcal endocarditis and colon cancer? *Clin Microbiol Infect*. 2008;14:190.
- Coffey S, Nadarasa K, Pan A, van der Linden A, Chu J, Schultz M. The increasing incidence of *Streptococcus bovis* endocarditis and bacteraemia: a case series from 1997 to 2010. *Int J Cardiol*. 2012;161:111–3.
- Hoen B, Chirouze C, Cabell CH, Selton-Suty C, Duchêne F, Olaison L, et al. Emergence of endocarditis due to group D streptococci: findings derived from the merged database of the International Collaboration on Endocarditis. *Eur J Clin Microbiol Infect Dis*. 2005;24:12–6.
- Corredoira J, Grau I, García-Rodríguez JF, Alonso-García P, García-País MJ, Rabuñal R, et al. The clinical epidemiology and malignancies associated with *Streptococcus bovis* biotypes in 506 cases of bloodstream infections. *J Infect*. 2015;71:317–25.
- Muñoz P, Kestler M, De Alarcon A, Miro JM, Bermejo J, Rodríguez-Abella H, et al. Current epidemiology and outcome of infective endocarditis: a multicenter, prospective, cohort study. *Medicine (Baltim)*. 2015;94:e1816.
- Corredoira J, García-País MJ, Rabuñal R, Alonso MP. *Streptococcus bovis* endocarditis: epidemiological differences depending on geographical source. *Am Heart J*. 2016;177:e1–2.
- Dumke J, Hinse D, Vollmer T, Schulz J, Knabbe C, Dreier J. Potential transmission pathways of *Streptococcus gallolyticus* subsp. *gallolyticus*. *PLoS One*. 2015;10:e0126507.
- Jans C, Meile L, Lacroix C, Stevens MJ. Genomics, evolution, and molecular epidemiology of the *Streptococcus bovis*/*Streptococcus equinus* complex (SBSEC). *Infect Genet Evol*. 2015;33:419–36.
- Lun ZR, Wang QP, Chen XG, Li AX, Zhu XQ. *Streptococcus suis*: an emerging zoonotic pathogen. *Lancet Infect Dis*. 2007;7:201–9.
- Bordes-Benítez A, Sánchez-Oñoro M, Suárez-Bordón P, García-Rojas AJ, Saéz-Nieto JA, González-García A, et al. Outbreak of *Streptococcus equi* subsp. *zooeconomicus* infections on the island of Gran Canaria associated with the consumption of inadequately pasteurized cheese. *Eur J Clin Microbiol Infect Dis*. 2006;25:242–6.
- Devriese LA, Laurier L, De Herdt P, Haesebrouck F. Enterococcal and streptococcal species isolated from faeces of calves, young cattle and dairy cows. *J Appl Bacteriol*. 1992;72:29–31.
- Gonzalez-Quintela A, Fernández-Conde S, Alves M[†]T, et al. Temporal and spatial patterns in the rate of alcohol withdrawal syndrome in a defined community. *Alcohol*. 2011;45:105–11.
- Ministerio de Medio Ambiente y Medio Rural y Marino. Secretaría general técnica. Subdirección general de estadística. <http://www.mapama.gob.es/es/estadistica/temas/estadisticas-agrarias>. Accessed 10 Feb 2018.
- Instituto Galego de Estatística. <http://www.ige.eu/igebdt/igeapi/datos/5230/0:2010,1:0,2:0,9915:12:15:27:32:36> Accessed 1 Dec 2017.
- Vergara-López S, de Alarcón A, Mateos-Gómez A, Georgieva RI, González-Nieto JA, Guerrero Sánchez F, et al. [Descriptive analysis of diseases associated with *Streptococcus bovis* bacteremia]. *Med Clin (Barc)*. 2011;137:527–32.
- Hoen B, Alla F, Selton-Suty C, Béguinot I, Bouvet A, Briançon S, et al. Changing profile of infective endocarditis: results of a 1-year survey in France. *JAMA*. 2002;288:75–81.
- Corredoira J, García-Garrote F, Rabuñal R, López-Roses L, García-País MJ, Castro E, et al. Association between bacteremia due to *Streptococcus gallolyticus* subsp. *gallolyticus* (*Streptococcus bovis* I) and colorectal neoplasia: a case control study. *Clin Infect Dis*. 2012;55:491–6.
- Romero B, Morosini MI, Loza E, Rodríguez-Baños M, Navas E, Cantón R, Campo RD. Reidentification of *Streptococcus bovis* isolates causing bacteremia according to the new taxonomy criteria: still an issue? *J Clin Microbiol*. 2011;49:3228–33.
- Dumke J, Vollmer T, Akkermann O, Knabbe C, Dreier J. Case-control study: Determination of potential risk factors for the colonization of healthy volunteers with *Streptococcus gallolyticus* subsp. *gallolyticus*. *PLoS One*. 2017;12:e0176515.

33. Actualitix. World Atlas. Statistics by country. <https://es.actualitix.com>. Accessed 10 Feb 2018.
34. Xunta de Galicia. Programa galego de prevención e control da tuberculose. Dirección Xeral de Saude Pública. Santiago de Compostela. 2017. <http://www.sergas.es/saude-publica>. Accessed 10 Feb 2018.
35. Marmolin ES, Hartmeyer GN, Christensen JJ, Nielsen XC, Dargis R, Skov MN, et al. Bacteremia with the *bovis* group streptococci: species identification and association with infective endocarditis and with gastrointestinal disease. *Diagn Microbiol Infect Dis*. 2016;85:239–42.
36. Papadimitriou K, Anastasiou R, Mavrogonatou E, Blom J, Papan-dreou NC, Hamdrakas SJ, et al. Comparative genomics of the dairy isolate *Streptococcus macedonicus* ACA-DC 198 against related members of the *Streptococcus bovis*/*Streptococcus equinus* complex. *BMC Genom*. 2014;15:272.
37. Lin IH, Liu TT, Teng YT, Wu HL, Liu YM, Wu KM, Chang CH, Hsu MT. Sequencing and comparative genome analysis of two pathogenic *Streptococcus gallolyticus* subspecies: genome plasticity, adaptation and virulence. *PLoS One*. 2011;6:e20519.
38. Rusniok C, Couvé E, Da Cunha V, El Gana R, Zidane N, Bouchier C, et al. Genome sequence of *Streptococcus gallolyticus*: insights into its adaptation to the bovine rumen and its ability to cause endocarditis. *J Bacteriol*. 2010;193:2266–76.
39. Jans C, Follador R, Hochstrasser M, Lacroix C, Meile L, Stevens MJ. Comparative genome analysis of *Streptococcus infantarius* subsp. *infantarius* CJ18, an African fermented camel milk isolate with adaptations to dairy environment. *BMC Genom*. 2013;14:200.
40. Schulz J, Dumke J, Hinse D, Dreier J, Habig C, Kemper N. Organic Turkey flocks: a reservoir of *Streptococcus gallolyticus* subspecies *gallolyticus*. *PLoS One*. 2015;10:e0144412.
41. Tsakalidou E, Zoidou E, Pot B, Wassill L, Ludwig W, Devriese LA, et al. Identification of streptococci from Greek Kasser cheese and description of *Streptococcus macedonicus* sp. nov. *Int J Syst Bacteriol*. 1998;48:519–27.
42. Jans C, Kaindi DW, Bock D, Njage PM, Kouamé-Sina SM, Bonfoh B, et al. Prevalence and comparison of *Streptococcus infantarius* subsp. *infantarius* and *Streptococcus gallolyticus* subsp. *macedonicus* in raw and fermented dairy products from East and West Africa. *Int J Food Microbiol*. 2013;167:186–95.
43. Lazarovitch T, Shango M, Levine M, Brusovansky R, Akins R, Hayakawa K, et al. The relationship between the new taxonomy of *Streptococcus bovis* and its clonality to colon cancer, endocarditis, and biliary disease. *Infection*. 2013;41:329–37.
44. Dumke J, Hinse D, Vollmer T, Knabbe C, Dreier J. Development and application of a multilocus sequence typing scheme for *Streptococcus gallolyticus* subsp. *gallolyticus*. *J Clin Microbiol*. 2014;52:2472–8.

Affiliations

J. Corredoira¹ · E. Miguez² · L. M. Mateo³ · R. Fernández-Rodríguez⁴ · J. F. García-Rodríguez⁵ · A. Pérez-González⁶ · A. Sanjurjo⁷ · M. V. Pulian⁸ · R. Rabuñal¹  · GESBOGA

J. Corredoira
juan.corredoira.sanchez@sergas.es

E. Miguez
Enrique.Miguez.Rey@sergas.es

L. M. Mateo
Lara.Maria.Mateo.Mosquera@sergas.es

R. Fernández-Rodríguez
ricardo.fernandez.rodriguez@sergas.es

J. F. García-Rodríguez
Jose.Francisco.Garcia.Rodríguez@sergas.es

A. Pérez-González
Alexandre.Perez.Gonzalez@sergas.es

A. Sanjurjo
asanjurjo@povisa.es

M. V. Pulian
victoria.pulian.morais@sergas.es

¹ Infectious Diseases Unit, Hospital Universitario Lucus Augusti, Lugo, Spain

² Infectious Diseases Unit, Complexo Hospitalario Universitario A Coruña, A Coruña, Spain

³ Internal Medicine, Complexo Hospitalario Universitario de Santiago, Santiago de Compostela, Spain

⁴ Infectious Diseases Unit, Complexo Hospitalario Universitario de Ourense, Ourense, Spain

⁵ Infectious Diseases Unit, Complexo Hospitalario Universitario de Ferrol, Ferrol, Spain

⁶ Internal Medicine, Complexo Hospitalario Universitario de Vigo, Vigo, Spain

⁷ Internal Medicine, Hospital POVISA, Vigo, Spain

⁸ Microbiology, Complexo Hospitalario Universitario de Pontevedra, Pontevedra, Spain