



Changing trends in β -hemolytic streptococcal bacteremia in Manitoba, Canada: 2007–2012



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SUMMARY

Objectives: European surveillance studies have reported an increasing incidence of β -hemolytic group G streptococcal bacteremia, but no studies have evaluated trends in β -hemolytic streptococcal bacteremia in North America.

Methods: We reviewed bacteremic episodes and positive throat swab cultures from two tertiary care centers in Manitoba, Canada, from January 2007 to December 2012.

Results: During the study period, 19 864 bacteremic episodes, and 9948 positive throat swabs were identified. There were 1025 (5.16%) bacteremic episodes attributable to β -hemolytic streptococci: 425 (2.03%), 339 (1.71%), 62 (0.31%), and 199 (0.95%) to β -hemolytic groups A, B, C, and G streptococci, respectively. From 2007 to 2012, there were significant increases in the proportion of bacteremia attributable to β -hemolytic streptococci in general (6.32% vs. 4.02%; $p < 0.0001$; linear trend test, $p < 0.0001$), and to groups G (1.49% vs. 0.43%; $p < 0.0001$; linear trend test, $p < 0.0001$) and C (0.58% vs. 0.13%; $p = 0.0068$; linear trend test, $p = 0.0105$) β -hemolytic streptococci in particular. Bacteremia attributable to groups A and B β -hemolytic streptococci and *Streptococcus pneumoniae* were unchanged. There were no changes in the distribution of β -hemolytic streptococcal groups among throat swabs.

Conclusions: Bacteremia attributable to β -hemolytic groups G and C streptococci increased in Manitoba, Canada. Further study of the factors underlying these changes is required.

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1. Introduction

β -Hemolytic streptococci cause skin and soft tissue infections, bacteremia, and post-infectious immune-mediated sequelae in humans. Bacteremia is relatively uncommon, but carries a grave prognosis.^{1–3} The β -hemolytic streptococci most commonly implicated in invasive human disease include Lancefield groups A (GAS), B (GBS), C (GCS), and G (GGs). Recent evidence has suggested changing epidemiology of these infections, most notably with GGS increasing in frequency, and in some centers surpassing GAS as the predominant cause of invasive β -hemolytic streptococcal infection.^{2,4}

To date, there have been no reports on the trends of invasive β -hemolytic streptococcal infections from North America. We hypothesized that the proportion of bacteremia attributable to GGS has been increasing, that changes in the proportion of bacteremia attributable to β -hemolytic streptococcal groups would be mirrored by changes in the proportion of those groups isolated from oropharyngeal specimens, and that these changes would be accompanied by a decrease in bacteremia attributable to *Streptococcus pneumoniae*.

2. Methods

Data were compiled from two tertiary care centers in Manitoba, Canada, for the period 2007 to 2012 in order to determine the frequency of bacteremia caused by GAS, GBS, GCS, and GGS. St. Boniface General Hospital and Health Sciences Centre are tertiary

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Table 1
Number of episodes of bacteremia attributable to β -hemolytic streptococci, *Streptococcus pneumoniae*, and the total from all organisms, and the number of clinically submitted throat swabs from which β -hemolytic streptococci were isolated, by group, 2007–2012

	Source							Throat swabs			
	Blood cultures										
	GAS (%)	GBS (%)	GCS (%)	GBS (%)	Total β HS (%)	<i>S. pneumoniae</i> (%)	Total episodes of bacteremia	GAS (%)	GCS (%)	GBS (%)	Total positive throat swabs
2007	58 (1.92)	46 (1.53)	4 (0.13)	13 (0.43)	121 (4.02)	73 (2.42)	3013	1575 (82.72)	131 (6.88)	198 (10.40)	1904
2008	53 (1.76)	44 (1.46)	10 (0.33)	23 (0.76)	130 (4.31)	78 (2.58)	3018	1200 (80.00)	128 (8.53)	172 (11.47)	1500
2009	85 (2.67)	44 (1.38)	5 (0.16)	27 (0.85)	161 (5.05)	94 (2.95)	3189	1428 (81.00)	144 (8.17)	191 (10.83)	1763
2010	71 (2.06)	76 (2.21)	11 (0.32)	30 (0.87)	188 (5.46)	141 (4.09)	3444	1134 (80.48)	124 (8.80)	151 (10.72)	1409
2011	74 (2.07)	59 (1.65)	11 (0.31)	52 (1.45)	196 (5.48)	105 (2.94)	3574	1355 (83.28)	149 (9.16)	123 (7.56)	1627
2012	84 (2.32)	70 (1.93)	21 (0.58)	54 (1.49)	229 (6.32)	133 (3.67)	3626	1488 (85.27)	139 (7.97)	118 (6.76)	1745
Total	425 (2.14)	339 (1.71)	62 (0.31)	199 (1.00)	1025 (5.16)	624 (3.14)	19 864	8180 (82.22)	815 (8.19)	953 (9.58)	9948

GAS, group A β -hemolytic streptococci; GBS, group B β -hemolytic streptococci; GCS, group C β -hemolytic streptococci; GGS, group G β -hemolytic streptococci; β HS, β -hemolytic streptococci.

care hospitals in Winnipeg, Manitoba, with a combined 1440 inpatient beds, serving a population of 1.2 million people in a catchment area including all of Manitoba and parts of western Ontario and the territory of Nunavut.

Where multiple blood cultures were positive for the same organism from the same patient within 6 months, only one was counted. Because of increased specimens processed through the study period, frequencies were calculated as a proportion of total positive blood cultures. The difference in annual relative proportions of groups was tested with a multinomial logistic model. Within each group, temporal changes were assessed using linear trend tests derived from logistic regression models with calendar year as the sole predictor. Post-hoc comparisons between years were also calculated for each model. Analyses were performed with SAS version 9.3 (SAS Institute, Cary, NC, USA).

Blood cultures were incubated using the BacT/ALERT 3D automated microbial detection system (bioMérieux, Marcy l'Etoile, France) with aerobic (BacT/ALERT FA) and/or anaerobic (BacT/ALERT FN) media, or BacT/ALERT pediatric FAN media. Positive blood culture bottles with Gram-positive cocci observed on Gram stain were plated to sheep's blood, chocolate, and Brucella with vitamin K agars, and incubated at 35 °C under aerobic, CO₂, or anaerobic conditions (in anaerobic jars with AnaeroGen gas-generating packs; Oxoid, Basingstoke, UK). Gram-positive cocci that were catalase-negative demonstrating β -hemolysis on blood agar were tested for latex agglutination using a PathoDX Strep Grouping Kit (Thermo Fisher Scientific, Lenexa, KS, USA) and the methylumbelliferyl β -glucuronide (MUG) test for GCS and GGS. Gram-positive cocci demonstrating α -hemolysis with colonies typical for *S. pneumoniae* were confirmed with a bile solubility test. These protocols are in accordance with Clinical and Laboratory Standards Institute guidelines.⁵

In order to determine if trends in β -hemolytic streptococcal bacteremia reflected changing trends in β -hemolytic streptococcal oropharyngeal infection, we also reviewed all throat swab cultures obtained during the study period. Throat swabs were inoculated to blood agar plates, incubated aerobically at 35 °C for 18–24 h, and any growth that appeared consistent with β -hemolytic streptococci (based on hemolysis pattern and colony morphology) was confirmed as *Streptococcus* using catalase; grouping was then done using latex agglutination and MUG tests.

3. Results and discussion

We reviewed 19 864 positive blood cultures, including 1025 (5.16%) episodes of bacteremia attributable to β -hemolytic streptococci (Table 1). Changes in the relative proportions of bacteremia attributable to β -hemolytic streptococci in total and by Lancefield grouping over the study period are shown in Figure 1A;

linear trends are displayed in Figure 1B. The proportion of bacteremia attributable to β -hemolytic streptococci increased significantly (2007 vs. 2012, $p < 0.0001$). There were significant increases in the proportion of bacteremia attributable to GCS (2007 vs. 2012, $p = 0.0068$) and GGS (2007 vs. 2012, $p < 0.0001$). There was no significant change in the proportion of bacteremia attributable to GAS (2007 vs. 2012, $p = 0.2729$) or GBS (2007 vs. 2012, $p = 0.2123$).

Our observation of an increase in bacteremia attributable to GGS is consistent with reports from Europe, where an increasing incidence of GGS bacteremia was observed in Finland from 1995 to 2004⁶ and in Denmark from 1999 to 2002⁷ and from 2005 to 2011,⁸ and also Jerusalem, Israel throughout the 1990s.⁴ Conversely,

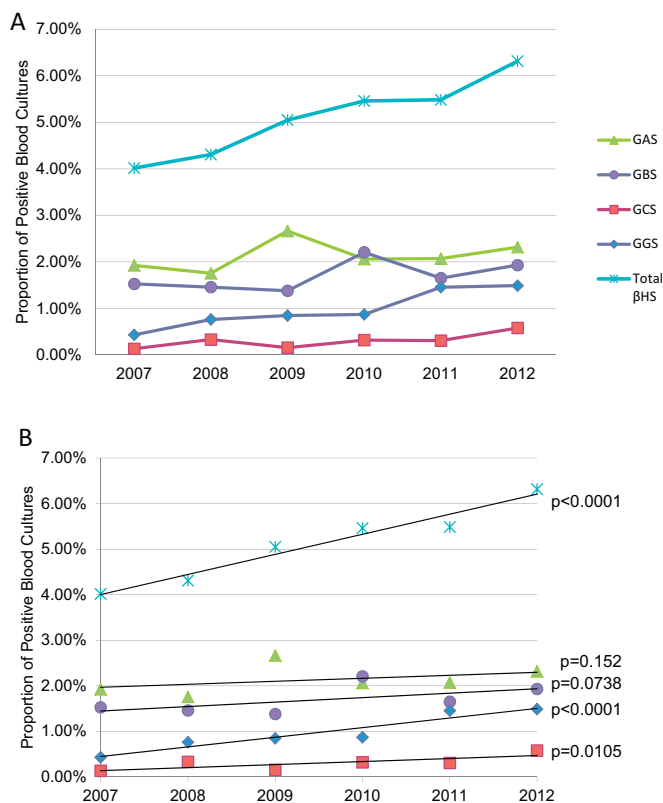


Figure 1. (A) Proportion of bacteremia attributable to β -hemolytic streptococci, in total and by Lancefield grouping, from 2007 to 2012; (B) with linear trends. (Abbreviations: GAS: β -hemolytic group A streptococci; GBS: β -hemolytic group B streptococci; GCS: β -hemolytic group C streptococci; GGS: β -hemolytic group G streptococci; β HS: β -hemolytic streptococci.)

stable rates of GGS bacteremia have been reported from another Jerusalem hospital over this same period,⁹ and from North Queensland, Australia from 1996 to 2000.¹⁰

Our finding of an increasing proportion of bacteremia attributable to GCS over the study period is consistent with the findings of a large national surveillance study from Denmark for the years 2005–2011.⁸ In contrast, most other investigators have reported no significant change,^{1,2,6,7,10,11} a discrepancy which may result from smaller studies being underpowered.

We further tested whether the observed changes were also associated with a decrease in *S. pneumoniae* bacteremia, perhaps related to an increased uptake of the *S. pneumoniae* conjugate vaccine, similar to the suggested inverse relationship of carriage between *Staphylococcus aureus* and *S. pneumoniae*.¹² We found no significant changes in the proportion of bacteremia caused by *S. pneumoniae* during the study period (2007 vs. 2012, $p = 0.0038$; linear trend test, $p = 0.1247$).

A total of 9948 throat swabs yielded isolates of GAS, GCS, or GGS (Table 1). There were no significant changes in the relative proportions of these bacteria isolated from positive throat swabs ($p = 1.0$, multinomial logistic model with year as predictor). Of note, GBS was not routinely reported because it does not cause pharyngitis. Furthermore, throat swabs would have been submitted on suspicion of clinical pharyngitis and thus may not truly reflect rates of asymptomatic carriage. Because throat swabs were not matched to blood cultures, inferences of the relationship between β -hemolytic streptococcal oropharyngeal and invasive disease were limited.

This study is, to our knowledge, the first to examine trends in β -hemolytic streptococcal bacteremia in North America, and is supported by a large sample size. There were no changes implemented to the methods of blood culture collection, incubation, or identification of the β -hemolytic streptococci. Along with trends reported elsewhere, this suggests that the changes observed

represent changing epidemiology in β -hemolytic streptococcal bacteremia.

Conflict of interest: The authors declare no conflicts of interest.

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