Research Article

Outbreak of Streptococcus pyogenes emm type 58 in a high dependency unit of a level-1 trauma center of India

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Abstract

Background and Aims: Group A *Streptococcus* (GAS) can cause illnesses ranging from self-limited to severe, life-threatening, invasive infections. The objective of the following study was to investigate a suspected *Streptococcus pyogenes* outbreak in a high dependency unit (HDU) of our trauma center. **Materials and Methods:** All the isolates of beta hemolytic Streptococci were identified by standard microbiological methods, Vitek 2 system and latex agglutination tests. Antimicrobial susceptibility testing was performed as recommended by Clinical Laboratory Standards Institute. Exotoxin genes, including *speA*, *speB*, *speC*, *speF*, *smeZ*, *ssa*, *speG*, *speH*, *speJ*, *speL*, *speM* and *speI* were detected by polymerase chain reaction (PCR). The *emm* types of isolates of *S. pyogenes* were determined by sequencing the variable 5' end of *emm* gene after amplification by PCR. **Results:** In a 28 bedded poly-trauma ward with a four bedded HDU three out of four patients developed *S. pyogenes emm* type 58 infection. The strain was macrolide and tetracycline resistant and produced the Streptococcal pyrogenic exotoxins *speB*, *speC*, *speG*, *speF* and *smeZ*. Surveillance sampling was done for investigation from patients, health-care workers and environmental samples. **Conclusion:** An outbreak of GAS infections was established caused by the uncommonly reported *emm* type 58. The outbreak was controlled by prompt treatment, intensive surveillance, feedback and training.

Keywords: Beta-hemolytic Streptococci, group A *Streptococcus*, outbreak, *Streptococcus* pyrogenic exotoxins *emm* types, trauma patients

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Introduction

Streptococcus pyogenes (group A *Streptococcus*; [GAS]) causes a range of clinical syndromes from mild pharyngitis to severe, life threatening toxic shock syndrome.[1] The M protein of GAS, encoded by the *emm* gene is a major virulence factors for the organism.[2] The high variability of the amino-terminus of the *emm* gene makes *emm* typing an excellent epidemiological marker, recommended as the "Gold standard" by the Centers for Disease Control and Prevention (CDC).[2,3] Invasive infections due to GAS have increased in the past two decades, presumably due to the emergence of virulent clones of a few *emm* types.[4] In October, 2012, a cluster of cases of invasive GAS infections was noted in a high dependency unit (HDU) of a level-1 trauma care center of India. This initiated an intensive surveillance and search for additional cases/carriers of the pathogen and institution of prompt treatment, which could control the outbreak. This report elaborates the epidemiological investigation and control measures of the outbreak. Sequence analysis of *emm* gene and profiling of exotoxin production was done, to ascertain the similarity and virulence of the strains.

Materials and Methods

All the isolates of beta-hemolytic Streptococci (βHS) were identified by standard microbiological methods.[5] The confirmation of identity was also done by the Vitek

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2 (Biomerieux, France). Grouping of the Streptococci was performed by agglutination test (HiMedia Labs, Mumbai, India) according to manufacturer's instructions. All the strains were stocked in stocking beads (Microbank™, Pro-Lab Diagnostics, Austin, Texas, USA) at −70°C till further analysis.

Exotoxin genes, including *speA*, *speB*, *speC*, *speF*, *smeZ*, *ssa*, *speG*, *speH*, *speJ*, *speL*, *speM* and *speI* were detected by polymerase chain reaction (PCR) as per published protocol.[6,7] Amplification of all the genes was performed with an initial 5 min denaturation at 94°C followed by 30 cycles of denaturation at 94°C for 30 s, 30 s of annealing at the appropriate temperature for each gene, as specified in Table 1 and 60 s of extension at 72°C with a final extension step at 72°C for 7 min. *S. pyogenes* ATCC strains 12351, 12344, 700294 and 51500 were used as controls.

The *emm* types of isolates of *S. pyogenes* were determined by sequencing the variable 5′ end of *emm* gene after amplification by PCR. For this, the DNA preparation of GAS strains was performed as described by the USA CDC. The amplification of *emm* gene and sequencing was performed as per the published protocol.[3] Amplification of the *emm* genes was performed by the "all M" primer having the following sequence:

- Forward primer: 5′-GGG GGG GGA TCC ATA AGG AGC ATA AAA ATG GCT-3′
- Reverse primer: 5′-GGG GGG GAA TTC AGC TTA GTT TTC TTC TTT GCG-3′.

The *emm* gene-specific amplicon was used as a template to determine the sequence of hypervariable region of *emm* gene. 30 ng of PCR product was sequenced by using primer (5′-ATAAGGAGCATAAAAATGGCT-3′) with the dye terminator mix and subjected to automated sequence analysis on autosequencer as per manufacturer's instructions. The cycling parameters were 96°C for 30 s, 50°C for 15 s and 60°C for 4 min. The *emm* gene sequence was subjected to homology search by Blast search analysis (http://www.ncbi.nlm.nih.gov/BLAST/Blast.cgi). A comparison of the nucleotide homology for the first 200 bases of the hypervariable region was conducted. Strains, which showed ≥95% homology with reference strain was designated the particular parental *emm* type. Types (based on variation in the type-specific region of *emm* gene) were designated according to the information available at CDC website (http://www.cdc.gov/ncidod/biotech/strep/doc.htm).

The sequences were submitted to GenBank and assigned sequence numbers.

The antimicrobial susceptibility testing of Streptococci was performed by the disk diffusion method on Mueller Hinton agar with 5% sheep blood according to the recommendations of the Clinical Laboratory Standards Institute (CLSI).[8,9] The following antibiotics were tested: Penicillin G, ampicillin vancomycin, erythromycin, clindamycin, cefotaxime, ceftriaxone, linezolid, teichoplanin, ciprofloxacin, levofloxacin, tetracycline

Table 1: Primers and conditions to be used for PCR of virulence genes

Gene	Primer direction	Primer sequence	Annealing temperature	Amplicon size
speA	Forward	5′-CGGAATCCATGTCAACAAGACCCAAGCCCAGC-3′	55°C	660 bp
	Reverse	5′-CGGGATCCTTACTTGGTTGTTAGGTAGAC-3′		
speB	Forward	5′-GTGGAGTCTCTGACGGCTTC-3′	50°C	170 bp
	Reverse	5′-GTGTTTTCGGCACAAAAGGT-3′		
speC	Forward	5′-GCGAATTCATGGACTCTAAGAAAGACATTTCG-3′	50°C	627 bp
	Reverse	5′-GCGGATCCTTATTTTCAAGATAAATATCG-3′		
speF	Forward	5′-CGAAATTAGAAAAGAGGAC-3′	57°C	1193 bp
	Reverse	5′-GGCTGAGCAAAAGTGTGTG-3′		
Ssa	Forward	5′-GTGCACAATTATTATCGATTAGTG-3′	60°C	723 bp
	Reverse	5′-GGTGAACCTCTATAGCTATAGCTGAAG-3′		
smeZ	Forward	5′-TAGAAGTAGATAATAATTCC-3′	48.3°C	629 bp
	Reverse	5′-TTAGGAGTCAATTTCTATAT-3′		
SpeG	Forward	5′-AGA AAC TTA TTT GCC C-3′	42°C	155 bp
	Reverse	5′-TAGTAGCAAGGAAAAGG-3′		
SpeH	Forward	5′-AGATTGGATATCACAGG-3′	42°C	416 bp
	Reverse	5′-CTATTC TCT CGT TAT TGG-3′		
SpeJ	Forward	5′-ATC TTT CAT GGG TAC G-3′	44°C	535 bp
	Reverse	5′-TTT CAT GTT TAT TGC C-3′		
SpeL	Forward	5′-TTAGGATGGTTTCTGCGGAAGAGAC-3′	60°C	596 bp
	Reverse	5′-TTCCTCTTTCTCGCCTGAGCCGTG-3′		
SpeM	Forward	5′-GCTCTATACACTACTGAGAGTGTC-3′	56°C	612 bp
	Reverse	5′-CATATCAATCGTTTCATTATCTG-3′		
SpeI	Forward	5′-ATGAGTAGTGTGGGAGTTATTAA-3′	50°C	678 bp
	Reverse	5′-TTATTTATTAAATTTAACTAAG-3′		

PCR: Polymerase chain reaction

and chloramphenicol. The CLSI recommended inhibition zone sizes for βHS were used for interpretation. *Streptococcus pneumoniae* ATCC 49619 was used as control for antimicrobial susceptibility testing. The minimum inhibitory concentration (MIC) was also determined by E-test for all the above antimicrobials. The E-test was performed on 5% sheep blood agar according to manufacturer's recommendations (Biomerieux Ltd., formerly AB Biodisk, Sweden).

PCR for *ermA*, *erm*B and *mef* A for detecting the macrolide resistance genes and *tet*M and *tet*O genes (for tetracycline resistance) was done by standard methods.[10,11]

The research work conducted in this investigation was part of an ongoing study on molecular epidemiology of Streptococci, which had received ethical clearance of the Institute's ethical committee.

Results

The outbreak and its investigation occurred in a 28-bedded poly-trauma ward of a level-1 Trauma Center. The ward has a four-bedded HDU [Figure 1]. On 9th October, 2012, the tracheal aspirate and blood sample of a patient (A) in the high dependency cubicle grew a beta hemolytic *Streptococcus*. The clinicians were immediately informed. The patient was in clinical sepsis and was very toxic. She had a C5 burst fracture and was on a ventilator since July, 2012. The patient was immediately started on clindamycin and amoxicillin/clavulinic acid. The next day, the isolate was identified as GAS, showing inducible resistance to clindamycin (clindamycin MIC 0.094 μg/ml; D-test positive). The antimicrobial treatment was therefore changed to vancomycin along with amoxicillin/clavulinic acid. The tracheal aspirates and blood on 10th October also grew GAS. On the 11th October, a wound sample of another patient from the HDU (patient B) grew GAS. Since the patient on adjacent bed (A) had GAS from multiple sources, a tracheal aspirate and blood sample was taken from this patient. The tracheal aspirate of this patient also grew GAS. The blood sample was sterile. This patient had cervical spine fracture in June 2012 and was on the ventilator since then. The patient was immediately started on vancomycin. On the 12th October, the central line tip of a patient (C) sent for microbiological culture grew GAS. This patient was shifted to the ward from the ICU the previous day and the central line was removed since it was not clinically required.

Since it was unusual to get GAS from two patients in a cubicle (4 Bedded HDU), an intensive surveillance was initiated on the 11th October to trace the source of GAS and to ascertain if the same strain was causing the infection. Since a patient outside the cubicle (C) had also grown GAS on 12th October, the surveillance was enhanced to cover the entire ward. A total of 146 samples were taken. Of these, 48 were throat swabs of nursing staff in all the shifts, 4 were throat swabs of the house keeping staff, 16 were throat swabs/tracheal aspirates of other admitted patients, five were throat swabs of various attendants of the patients and 73 were environmental samples of various devices/surfaces in the wards.

Of these 146 samples, the ventilator tubing of patient B grew GAS. Apart from this, the tracheal aspirate and the tip of the suction tubing of another patient (patient D) grew GAS. This patient was a 2-year-old female, admitted to the ward since 1st August and was about to be discharged on the same day that surveillance samples were taken. Since GAS grew from her samples, she was kept in the ward and treated with amoxicillin/clavulinic acid. Her blood cultures were sterile and she was discharged after 2 days. A throat swab taken from this baby's mother also grew GAS. She was also treated with amoxicillin/clavulinic acid. The repeat samples of

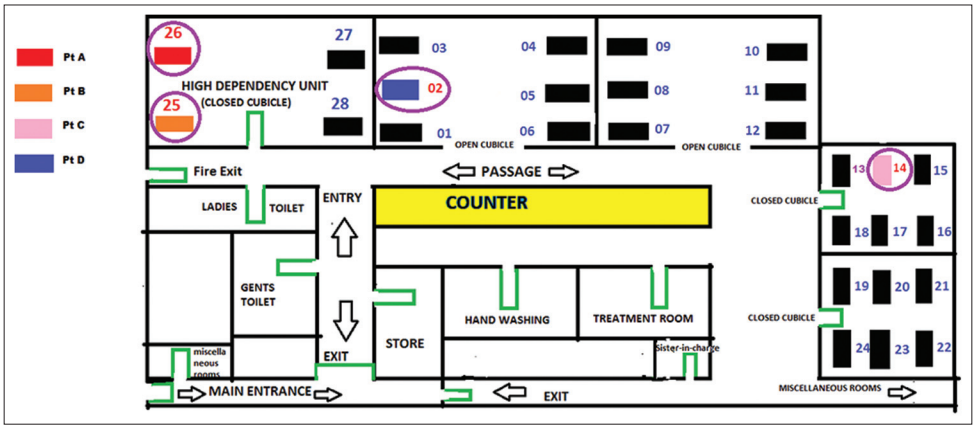

Figure 1: Ward layout

all the above patients after 5 days were sterile. However, on 21st October, the blood sample of patient B again grew GAS, which was immediately treated with vancomycin. None of the other samples from this patient or the surveillance samples taken this time grew GAS. From 21st October to 31st December, no further cases of infections due to GAS were seen in the ward. None of patients from whom GAS was isolated had a fatal outcome until 1-month follow-up.

PCR done for detection of exotoxins *speA, speB, speC, speF, speG, speI, speH, speL, speJ speM, smeZ and ssa* revealed that all the isolates of GAS obtained from the various sources produced *speB*, *speC*, *speG*, *speF* and *smeZ*. However, none of them produced *speA, speI, speM*, *speH*, *speL*, *speJ* or *ssa*, suggesting that they were the same clone.

A sequence analysis of the *emm* gene was done for all the isolates recovered during this period. All the isolates belonged to GAS *emm* type 58 (GenBank accession numbers KC352715-KC352726).

All the isolates were sensitive to penicillin (MIC: 0.012-0.016 μg/ml), cefotaxime (MIC: 0.016-0.023 μg/ml), ceftriaxone (MIC: 0.016 μg/ml), ciprofloxacin (MIC: 0.38-0.75 μg/ml), vancomycin (MIC: 0.38 μg/ml) and linezolid (MIC: 0.19-0.38 μg/ml). They were resistant to erythromycin (MIC: ≥256 μg/ml) and had inducible clindamycin resistance (D-test positive, clindamycin MIC: 0.094-0.19). They were also resistant to tetracycline (MIC: 64 μg/ml). There was very little variation in the MICs of the isolates obtained from different sources. All the isolates were positive for *erm*B and *tet*M genes. They were negative for *erm*A, *mef* A and *tet*O genes.

The strain was very invasive, considering that it was isolated from blood samples of two patients. Moreover, in two patients, it was isolated from multiple sources [Table 2].

None of the health care workers grew GAS. Only one nursing staff had a beta-hemolytic *Streptococcus* from her throat, which was identified as *Streptococcus dysgalactiae*. Since three of the four patients from whom GAS was recovered were admitted to the ward for a long time and none of the health care worker were found to carry the GAS strain, we can only speculate that the strain was introduced to the ward through the mother of patient D (since the same *emm* type was recovered from her throat) and spread through the ward due to suboptimal hand hygiene/infection control measures. We have an intensive, automated ongoing hospital acquired infection surveillance network and hand hygiene monitoring system.[12,13] The hand hygiene compliance for the months of September and October were respectively 64% and 73%. Since the isolate was obtained from suction tips and catheter tips, there was a definite lapse in infection control precautions in the ward. One of the reasons could be the involvement of patient's attendants in tracheal/oral suctioning, without being properly trained and not being monitored by staff. Suboptimal disinfection/cleaning of devices, which is done by house-keeping staff may also be a factor contributing to cross-transmission of the pathogen.

The nursing staff was thoroughly sensitized about the need to augment the implementation of infection preventive measures. Training of new recruits is being continuously done on all aspects of hospital infection control.

Discussion

This is the first reported outbreak of M type 58 GAS. No study from India on invasive/non-invasive GAS has reported finding of *emm* 58.[14-16] In an ongoing study on molecular epidemiology of GAS at our Center, we have found that of the 126 invasive and non-invasive GAS strains from north and south India, there was only one *emm* 58 isolate (unpublished data). In this ongoing study, from January, 2007 to June, 2012, a total of 85 isolates of βHS were isolated from trauma patients. Of these, four were recovered from blood (only one of which was GAS, rest being GGS). All these four patients had a fatal outcome.

Emm 58 was not found in many large-scale studies from Nepal, China, Taiwan, USA and Serbia.[17-20] Studies from

Table 2: Sources of GAS and their clinical significance

Patient	Samples growing GAS	Clinical condition	Treatment	Outcome
A	Blood, wound aspirate, tracheal aspirate, throat	Patient in clinical sepsis	Vancomycin	Recovered and discharged
B	Blood, tracheal aspirate, throat	Patient in clinical sepsis	Vancomycin	Recovered and discharged
C	Central line tip	Patient stable	Amoxicillin/clavulinic acid	Recovered and discharged
D	Tracheal aspirate, tip of suction tubing	Patient stable and was about to be discharged	Amoxicillin/clavulinic acid	Recovered and discharged

GAS: Group A *Streptococcus*

Italy, Denmark, Argentina, Australia and Canada have found a very low prevalence (0.5-3%) of *emm* 58 amongst all GAS isolates.[21-25] It is probably most prevalent in Japan, where it has been reported to account for 13-38% of the isolates in various studies.[26,27]

Hospital acquisition of invasive GAS infections has often been reported in the literature. In a meta-analysis from 1992 to 2000 in Canada, fifteen outbreaks were identified; 9 (60%) of them involving only two cases. Hospital staff were infected in 1 of the 15 outbreaks, but colonized staff were identified in 6 (60%) of the 10 investigations in which staff were screened.[28] GAS outbreaks have been identified in burns units, closed communities and long-term acute care hospitals.[29-31] However, to the best of our knowledge, this is the first outbreak in a trauma care set-up, which houses highly susceptible, predominantly young adult population.

In most of the reported outbreaks of GAS, multiple *emm* types have been observed,[32-35] suggesting multiple sources. However, in our study, a single *emm* type was isolated from all cases, suggesting a single source and cross-transmission. The isolate was a very virulent and invasive strain as it was isolated from blood culture and multiple sites of two patients both of them had a spinal injury. Three out of the four patients involved in this outbreak were admitted in the hospital for a prolonged time.

The *Streptococcus* pyrogenic exotoxins (SPEs) of GAS play an important role in its pathogenesis. The isolates in this outbreak produced *spe*B, *spe*C, *speG, speF* and *smeZ*. *speC* is carried on mobile elements and can be easily mobilized by lysogenic phages into non-toxigenic strains, facilitating dissemination of toxigenicity.[36]

The major limitation of our study was that we could not ascertain the actual source of the outbreak. Therefore, we could not undertake specific measures for source control. We could have been more aggressive in taking surveillance samples from naso-pharynx, scalp, per-vaginal and peri-anal etc., of the patients, as they have been implicated as possible sources of colonization and infection in earlier reported Streptococcal outbreaks. The doctors taking care of these patients are on daily rotation and they work in different shifts, which was a major hindrance in collecting surveillance samples from the doctors. However, we tried to take surveillance swabs from as many patients and their attendants and health care workers as possible. The best possible intervention in this situation of uncertainty was that all the colonized or infected patients, attendants and health care staff were treated with antibiotics along with enhanced hand hygiene and other hospital infection control practices.

Considering the high mortality of beta-hemolytic Streptococcal bacteremia, as observed in our set-up (unpublished data), we feel that we could control this outbreak through intensive surveillance, prompt treatment, attempted source tracing, molecular characterization, training and feedback.

References

1. Musser JM, Shelburne SA 3rd. A decade of molecular pathogenomic analysis of group A *Streptococcus*. J Clin Invest 2009;119:2455-63.
2. Efstratiou A. Group A Streptococci in the 1990s. J Antimicrob Chemother 2000;45 Suppl:3-12.
3. Beall B, Facklam R, Thompson T. Sequencing emm-specific PCR products for routine and accurate typing of group A Streptococci. J Clin Microbiol 1996;34:953-8.
4. Ekelund K, Skinhøj P, Madsen J, Konradsen HB. Reemergence of emm1 and a changed superantigen profile for group A Streptococci causing invasive infections: Results from a nationwide study. J Clin Microbiol 2005;43:1789-96.
5. Collee JG, Diguid JP, Fraser AG. Mackie and Mc Cartney Practical Medical Microbiology. 14th ed. Edinburgh: Churchill Livingstone; 1996.
6. Jing HB, Ning BA, Hao HJ, Zheng YL, Chang D, Jiang W, *et al*. Epidemiological analysis of group A Streptococci recovered from patients in China. J Med Microbiol 2006;55:1101-7.
7. Rivera A, Rebollo M, Miró E, Mateo M, Navarro F, Gurguí M, *et al*. Superantigen gene profile, emm type and antibiotic resistance genes among group a *Streptococcal* isolates from Barcelona, Spain. J Med Microbiol 2006;55:1115-23.
8. Clinical and Laboratory Standards Institute. Performance Standards for Antimicrobial Susceptibility Testing, 16th Informational Supplements, M100-S16. Wayne, PA, USA: CLSI; 2006.
9. Clinical Laboratory Standards Institute. Performance Standards for Antimicrobial Susceptibility Testing, 19th Informational Supplement. Vol. 29. Wayne, PA, USA: 2009.
10. Bingen E, Fitoussi F, Doit C, Cohen R, Tanna A, George R, *et al*. Resistance to macrolides in *Streptococcus pyogenes* in France in pediatric patients. Antimicrob Agents Chemother 2000;44:1453-7.
11. Ayer V, Tewodros W, Manoharan A, Skariah S, Luo F, Bessen DE. Tetracycline resistance in group a Streptococci: Emergence on a global scale and influence on multiple-drug resistance. Antimicrob Agents Chemother 2007;51:1865-8.
12. Gunjiyal J, Thomas SM, Gupta AK, Sharma BS, Mathur P, Gupta B, *et al*. Device-associated and multidrug-resistant infections in critically ill trauma patients: Towards development of automated surveillance in developing countries. J Hosp Infect 2011;77:176-7.
13. Mathur P, Jain N, Gupta A, Gunjiyal J, Nair S, Misra MC. Hand hygiene in developing nations: Experience at a busy level-1 trauma center in India. Am J Infect Control 2011;39:705-6.
14. Menon T, Whatmore AM, Srivani S, Kumar MP, Anbumani N, Rajaji S. EMM types of *Streptococcus pyogenes* in Chennai. Indian J Med Microbiol 2001;19:161-2.
15. Sagar V, Bakshi DK, Nandi S, Ganguly NK, Kumar R, Chakraborti A. Molecular heterogeneity among north Indian isolates of group a *Streptococcus*. Lett Appl Microbiol 2004;39:84-8.
16. Dey N, McMillan DJ, Yarwood PJ, Joshi RM, Kumar R, Good MF, *et al*. High diversity of group a *Streptococcal* EMM types in an Indian community: The need to tailor multivalent vaccines. Clin Infect Dis 2005;40:46-51.
17. Sakota V, Fry AM, Lietman TM, Facklam RR, Li Z, Beall B. Genetically diverse group a Streptococci from children in far-western Nepal share high genetic relatedness with isolates from other countries. J Clin Microbiol 2006;44:2160-6.
18. Shulman ST, Stollerman G, Beall B, Dale JB, Tanz RR. Temporal

changes in *Streptococcal* M protein types and the near-disappearance of acute rheumatic fever in the United States. Clin Infect Dis 2006;42:441-7.
19. Su YF, Wang SM, Lin YL, Chuang WJ, Lin YS, Wu JJ, *et al*. Changing epidemiology of *Streptococcus pyogenes* EMM types and associated invasive and noninvasive infections in Southern Taiwan. J Clin Microbiol 2009;47:2658-61.
20. Tanaka D, Gyobu Y, Kodama H, Isobe J, Hosorogi S, Hiramoto Y, *et al*. EMM typing of group A *Streptococcus* clinical isolates: Identification of dominant types for throat and skin isolates. Microbiol Immunol 2002;46:419-23.
21. Ekelund K, Darenberg J, Norrby-Teglund A, Hoffmann S, Bang D, Skinhøj P, *et al*. Variations in emm type among group A *Streptococcal* isolates causing invasive or noninvasive infections in a nationwide study. J Clin Microbiol 2005;43:3101-9.
22. Lopardo HA, Vidal P, Sparo M, Jeric P, Centron D, Facklam RR, *et al*. Six-month multicenter study on invasive infections due to *Streptococcus pyogenes* and *Streptococcus* dysgalactiae subsp. equisimilis in Argentina. J Clin Microbiol 2005;43:802-7.
23. Harris P, Siew DA, Proud M, Buettner P, Norton R. Bacteraemia caused by beta-haemolytic Streptococci in North Queensland: Changing trends over a 14-year period. Clin Microbiol Infect 2011;17:1216-22.
24. Creti R, Imperi M, Baldassarri L, Pataracchia M, Recchia S, Alfarone G, *et al*. EMM types, virulence factors, and antibiotic resistance of invasive *Streptococcus pyogenes* isolates from Italy: What has changed in 11 years? J Clin Microbiol 2007;45:2249-56.
25. Tyrrell GJ, Lovgren M, Forwick B, Hoe NP, Musser JM, Talbot JA. M types of group a *Streptococcal* isolates submitted to the National Centre for *Streptococcus* (Canada) from 1993 to 1999. J Clin Microbiol 2002;40:4466-71.
26. Tanaka D, Isobe J, Kimata K, Shima T, Watahiki M. Molecular analysis of *Streptococcal* pyrogenic exotoxin genes among group A *Streptococcus* isolates from Japanese patients with pharyngitis and skin infections. Kansenshogaku Zasshi 2005;79:443-50.
27. Murakami J, Kawabata S, Terao Y, Kikuchi K, Totsuka K, Tamaru A, *et al*. Distribution of EMM genotypes and superantigen genes of *Streptococcus pyogenes* isolated in Japan, 1994-9. Epidemiol Infect 2002;128:397-404.
28. Daneman N, McGeer A, Low DE, Tyrrell G, Simor AE, McArthur M, *et al*. Hospital-acquired invasive group a *Streptococcal* infections in Ontario, Canada, 1992-2000. Clin Infect Dis 2005;41:334-42.
29. Jordan HT, Richards CL Jr, Burton DC, Thigpen MC, Van Beneden CA. Group a *Streptococcal* disease in long-term care facilities: Descriptive epidemiology and potential control measures. Clin Infect Dis 2007;45:742-52.
30. Deutscher M, Schillie S, Gould C, Baumbach J, Mueller M, Avery C, *et al*. Investigation of a group A *Streptococcal* outbreak among residents of a long-term acute care hospital. Clin Infect Dis 2011;52:988-94.
31. Gruteke P, van Belkum A, Schouls LM, Hendriks WD, Reubsaet FA, Dokter J, *et al*. Outbreak of group a Streptococci in a burn center: Use of pheno-and genotypic procedures for strain tracking. J Clin Microbiol 1996;34:114-8.
32. Mylvaganam H, Bruun T, Vindenes HA, Langeland N, Skrede S. Molecular epidemiological investigation of an outbreak of invasive beta-haemolytic *Streptococcal* infection in western Norway. Clin Microbiol Infect 2009;15:245-52.
33. Thigpen MC, Thomas DM, Gloss D, Park SY, Khan AJ, Fogelman VL, *et al*. Nursing home outbreak of invasive group a *Streptococcal* infections caused by 2 distinct strains. Infect Control Hosp Epidemiol 2007;28:68-74.
34. Erdem G, Abe L, Kanenaka RY, Pang L, Mills K, Mizumoto C, *et al*. Characterization of a community cluster of group a *Streptococcal* invasive disease in Maui, Hawaii. Pediatr Infect Dis J 2004;23:677-9.
35. Centers for Disease Control and Prevention (CDC). Invasive group A *Streptococcus* in a skilled nursing facility – Pennsylvania, 2009-2010. MMWR Morb Mortal Wkly Rep 2011;60:1445-9.
36. Lloyd C, Balakrishnan N, Menon T. Vir types of *Streptococcus pyogenes* in Chennai, South India. J Med Microbiol 2008;57:1176-7.

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