

## ***Streptococcus Milleri* Is Not an Uncommon Pyogenic Pathogen**

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**Background:** Members of *Streptococcus milleri* group (SMG) may be unrecognized or misidentified in many laboratories, and their clinical role in causing invasive pyogenic infections may be underestimated.

**Objective:** To study the bacteriological, antimicrobial susceptibility, and clinical significance of *Streptococcus milleri* (SMG).

**Design:** A prospective study.

**Setting:** King Hussein Medical Centre, Amman, Jordan.

**Method:** Seventy-three SMG isolated between November 2003 to October 2006 were examined. The phenotypic characteristics and hemolytic patterns of the bacterial colonies were noted. Lancefield sero-grouping was determined by rapid latex agglutination slide test. All isolates were tested using Vitek GPI System for identification. Antimicrobial susceptibility testing was performed by both disk diffusion method and Vitek GPS System. The clinical conditions associated with SMG isolates were recorded.

**Result:** All SMG colonies consistently produced characteristic caramel-like odor. They showed variable hemolysis and sero-grouping patterns. Forty (54.8%) isolates were non-hemolytic. Forty-One out of 73 (56.2%) were non-groupable. Only 13 (17.8%) isolates were identified by the Vitek GPI system. SMG isolates were resistant to gentamicin but sensitive to all the other tested antimicrobial agents. Cervical abscess was the commonest clinical presentation in this study.

**Conclusion:** SMG is a significant cause of serious invasive infections. Awareness of SMG by microbiologists and clinicians is important and may aid in laboratory and clinical diagnosis and better patient management. This is the first report from Jordan demonstrating the bacteriological, antimicrobial susceptibilities, and clinical significance of 73 isolates in our hospital.

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*Streptococcus milleri* is a large group (SMG) of heterogenous streptococci, which includes *Streptococcus angiosus*, *Streptococcus intermedius*, and *Streptococcus constellatus*<sup>1</sup>.

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The species name *Streptococcus angiosus* has recently been recognized as the approved official name of these organisms. The members of this group, although basically similar, show variable hemolysis patterns, growth properties, biochemical, and Lancefield serologic antigenic reactions. The SMG may be unrecognized or misidentified in many laboratories due to the lack of uniformity in taxonomy and speciation, and difficulties in microbiological identification. Conventional methods for species differentiation based on morphological observations, biochemical reactions, and sero-grouping are time-consuming, and the results are usually unsatisfactory<sup>2</sup>. A diagnostic caramel-like odor, due to the formation of the diacetyl metabolite is characteristically associated with agar cultures of SMG. The modern molecular methods including polymerase chain reaction (PCR) and restriction fragment length polymorphism (RFLP) have been used to identify species and proved to be rapid and reliable<sup>3</sup>. The SMG organisms have been considered harmless commensals that form part of the normal flora most commonly found in the mouth, throat, and gastrointestinal and genital tracts. However, SMG could be an aggressive pathogen causing invasive pyogenic infections with abscess formation and serious complications at various sites in the body including the heart, abdomen, central nervous system, and head and neck<sup>4,5,6</sup>. Although it has been shown that members of SMG are of different clinical importance and are not equally associated with abscess formation, clinicians need to recognize that these microorganisms as a group are able to cause serious purulent infections that may require prolonged treatment and surgical drainage<sup>7</sup>.

Normal flora such as SMG may become an important pathogen due to the current widespread use of antibiotics and the imbalance between organisms and host defenses. The detailed pathogenesis of SMG remains to be clarified; however, the production of many tissue-destroying enzymes such as collagenase and hyaluronidase, the massive release of cytokines through T cell response to certain exotoxins produced by SMG, and the co-existence with other microbes such as *Eikenella corrodens* and anaerobes have been suggested as important pathogenesis mechanisms<sup>8</sup>.

This is the first study from Jordan demonstrating the bacteriological characteristics, antimicrobial susceptibilities, and clinical significance of SMG.

## **METHOD**

A total of 73 SMG strains isolated in Princess Iman Research and Laboratory Sciences Centre, King Hussein Medical Centre, during 3-year period (from November 2003 to October 2006) were included in this study. The phenotypic characteristics were studied by examining pure separate colonies grown on blood and chocolate agars (Blood agar base - special, Mast Diagnostics, Merseyside, UK) after 24-48 hours of incubation at 37° C in an aerobic atmosphere with 5% carbon dioxide. Lancefield sero-grouping was performed by rapid latex agglutination slide test using Maststrep RST 201 (Mast Diagnostics, Merseyside, UK) according to manufacturer's instructions. All isolates were also tested using Vitek GPI System (bioMérieux, Durham, NC) for identification.

Disk diffusion antimicrobial susceptibility testing was performed according to the recommendations of the Clinical and Laboratory Standards Institute (CLSI) using ten antimicrobial disks (Oxoid, Hants, UK); penicillin G (2IU), ampicillin (10µg), amoxicillin/clavulanic acid (20/10µg), cefazolin (30µg), erythromycin (10µg), gentamicin (10µg), ceftriaxone (30µg), lincomycin (2µg), vancomycin (30µg) and teicoplanin (30µg). Vitek GPS System was also used for sensitivity testing<sup>9</sup>.

## RESULT

All SMG organisms were primarily isolated in pure cultures except for 4 (5.5%) strains, which were mixed with other Gram-negative rods. All the isolated strains formed minute colonies producing the characteristic caramel-like odor. Forty (54.8%) isolates were non-hemolytic, 26 (35.6%) alpha-hemolytic, and 7 (9.6%) beta-hemolytic. A total of 23 (31.5%) isolates belonged to Lancefield group F, 6 (8.2%) to group C, 3 (4.1%) to group G, and 41 (56.2%) were non-groupable. Only 13 (17.8%) isolates were identified by the Vitek system (GPI) at  $\geq 95\%$  confidence. SMG isolates were resistant to gentamicin but sensitive to all the other nine antimicrobial agents as tested by both disk diffusion method and Vitek GPS System.

## DISCUSSION

The SMG isolates examined in this study showed variable hemolysis patterns and Lancefield sero-grouping reactions, however the production of caramel-like odor by agar cultures of these organisms was consistent. We also report a poor identification rate (17.8%) of the isolates using the automated Vitek system (GPI). Therefore, awareness of SMG by microbiologists is important and may aid in the accurate and rapid laboratory identification based upon conventional diagnostic criteria.

The broad clinical spectrum of SMG infections in this institution was demonstrated, see table 1.

**Table 1: SMG-associated clinical conditions**

Clinical presentation	No
Cervical abscess	12
Superficial skin infection	11
Pelvic abscess	8
Brain abscess	7
Para-spinal abscess	6
Orbital abscess	5
Bacteremia	5
Pulmonary abscess and empyema	5
Liver abscess	4
Bartholin cyst abscess	4
Perianal abscess	2
Axillary abscess	1
Breast abscess	1
Colonic abscess	1
Pancreatic abscess	1

The cervical and para-spinal abscesses caused by SMG in this study were clinically mimicking tuberculous infections; however, other studies showed that SMG should be considered in the differential diagnosis of fungal infections<sup>10</sup>. Although no antimicrobial resistance, other than to gentamicin was detected in the SMG isolates, different trends in antimicrobial susceptibility were reported elsewhere<sup>11</sup>. Synergy between aminoglycosides and  $\beta$ -lactam agents can usually be demonstrated; therefore, their use in combination is a reasonable therapeutic practice. Awareness of SMG by clinicians is also important and may aid in the proper clinical diagnosis and management.

## CONCLUSION

**We conclude that SMG is a group of important pathogens that require close cooperation between microbiologists and clinicians for early diagnosis and proper treatment. Further studies are required to characterize these organisms and investigate their pathogenic mechanisms and clinical roles.**

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