

Group A Streptococcal bacteraemia

Experience at King Fahad Medical City in Riyadh, Saudi Arabia

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ABSTRACT

الأهداف: تحديد العرض السريري، والعوامل المؤدية، والنتيجة في المرضى الذين يعانون من مجموعة البكتيريا العقدية.

الطريقة: أجريت دراسة بأثر رجعي على 33 مريضاً للأطفال والكبار مع بكتيريا البكتيريا العقدية المقيحة ادخلوا مدينة الملك فهد الطبية، الرياض، المملكة العربية السعودية خلال الفترة من 2007م إلى 2015م.

النتائج: تم استعراض 33 سجلات المرضى، وتوثيق تجربتهم الدم مع المجموعة A العقدية الانحلالي بيتا. حوالي 51.5% من الأطفال و 48.5% من المرضى البالغين، مع نسبة الذكور إلى الإناث من 2:1. وكانت أكثر المضاعفات المبلغ عنها شيوها هي القصور الكلوي (45.5%) ومتلازمة الجهاز التنفسي الحادة (21.2%)، تليها العدوى الموضعية (15.2%)، الأنصباب الجنبي (6.1%)، الخراج (9.1%)، التهاب اللقافة الناخر (9.1%)، والتهاب المفاصل انتاني، والتهاب العظم والنقي (3%). كانت هناك 10 أحداث للصدمات: 6 كانت في طب الأطفال و4 في المرضى البالغين. في نهاية فترة الدراسة، توفي 12.1% من المرضى من المرض، 81.1% تعافى من المرض مع عدم وجود عقابيل، في حين تعافى 6.1% مع مرض. وقد لوحظت الوفيات في 4 المرضى؛ منهم 3 من مرضى الأطفال وواحد من البالغين الذين يعانون من حالات مرضية مشتركة.

الخاتمة: لقد لاحظنا تغييراً طفيفاً في نمط المرض على مدى 28 عاماً في المملكة العربية السعودية. تعتمد إدارة عدوى GAS الجائره على التشخيص الدقيق في الوقت المناسب مع الاستخدام المناسب للعلاج المضاد للميكروبات. تظهر أعلى المخاطر أن تكون ذات صلة بالمرض المزمن. من المعروف أن المجموعة A الغائرة العدوى العقدية لديها ذات معدل وفيات عالي.

Objectives: To identify clinical presentation, predisposing factors, and the outcome in patients with Group A Streptococcal bacteremia.

Methods: This is a retrospective study of 33 pediatric and adult patients with *Streptococcus pyogenes*

bacteremia, admitted at King Fahad Medical City, Riyadh, Kingdom of Saudi Arabia from 2007 to 2015.

Results: Thirty-three patient records, documenting bacteremia with group A beta-hemolytic streptococcus, were reviewed. Approximately 51.5% were pediatric and 48.5% were adult patients, with a male to female ratio of 2:1. The most frequently reported complications were renal impairment (45.5%) and acute respiratory distress (21.2%), followed by localized infection (15.2%), pleural effusion (6.1%), abscess (9.1%), necrotizing fasciitis (9.1%), septic arthritis, and osteomyelitis (3%). There were 10 episodes of shock: 6 were in pediatric and 4 were in adult patients. At the end of the study period, 12.1% patients died from the illness, 81.1% recovered from illness with no sequelae, while 6.1% recovered with sequelae. Mortality was observed in 4 patients; of them, 3 were pediatric patients and one was an adult with co-morbidities.

Conclusions: We have noted a minimal change in the disease pattern over the 28 years in Saudi Arabia. The management of invasive GAS infection depends on an accurate and timely diagnosis with an appropriate use of antimicrobial therapy. The highest risks appear to be related to chronic illness. Invasive Group A Streptococcal infection is known to have a high mortality rate.

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Invasive infections caused by group A *Streptococcus* (GAS) or *Streptococcus pyogenes* include sepsis, bacteremic pneumonia, necrotizing fasciitis (NF), and streptococcal toxic shock syndrome (STSS). Group A *Streptococcus* also causes noninvasive disease, most commonly manifested as pharyngitis, suppurative complications, such as otitis media, and nonsuppurative sequelae such as acute rheumatic fever and acute glomerulonephritis. Group A *Streptococcus* infection causes a significantly high morbidity and mortality with an estimated 500,000 deaths worldwide. Most of them could be attributed to an invasive infection, acute rheumatic fever, and subsequent rheumatic heart disease.^{1,2} Over the past 3 decades, the invasive infections of *Streptococcus pyogenes* have increased worldwide, which could be attributed to the emergence of new virulent strains.³⁻⁸ Case fatality ranges from 10% to 80% despite adequate management.^{8,9} The local data from Saudi Arabia show a case fatality rate ranging from 16% to 21%.^{10,11}

The objective of this study was to review the demographic data, clinical presentation, predisposing factors, and clinical outcomes of Group A streptococcal bacteremia and to assess pattern changes in the disease over 28 years in Saudi Arabia.

Methods. This was a retrospective study that recruited all patients who were admitted to King Fahad Medical City (KFMC), Riyadh, Saudi Arabia, between January 2007 and January 2015. King Fahad Medical City is a tertiary care center receiving referrals from all regions of the Kingdom of Saudi Arabia with a bed capacity of more than 1000. Patients, whose blood culture showed the growth of group A streptococcal organism, were included. Pediatric, as well as adult, patients were considered. Patients were excluded if they were discharged against medical advice, those with one visit to the emergency room, who failed to appear for a follow-up, and who were non-eligible, and transferred to other private hospitals after stabilization. The study was approved by the institutional review board at KFMC.

The medical records of patients diagnosed with group A beta-hemolytic streptococcal bacteremia were reviewed. A database comprising of demographic data, clinical manifestation, co-morbidities, laboratory

data, and the outcome was created. The occurrence of Group A beta-hemolytic streptococcal was considered as bacteremia when the organism was cultured from at least one occasion from the blood. Outcomes such as either death or discharge and neurological examination for the adult group were also recorded.

Statistical analysis. Data were collected and stored in a spreadsheet using Microsoft Excel 2010® software. The data management and coding were also carried out in Excel. Data were analyzed using SPSS® version 20.0 (IBM Inc., Chicago, Illinois, USA). The descriptive analysis was for the categorical variables and the data are presented in the form of frequencies and percentages.

Results. During the study period, a total of 33 patients were reviewed that had documented bacteremia with group A beta-hemolytic streptococcus. They constituted 17 (51.5%) pediatric patients and 16 (48.5%) adult patients, with a male to female ratio of 2:1 in both groups. The range of adult patients was 14 to 79 years with a median of 59 years and for children 1 month to 14 years with a median of 4 years. Cardiac disease were higher comorbidities rate in the sample included congestive heart failure, hypertension, coronary artery disease, congenital heart disease and rheumatic fever; malignancy; diabetes mellitus; immune-suppressive treatment; had prior recent trauma; prior recent influenza infection; prior recent surgery or procedure; and prior recent antibiotic use; liver disease was noted; prior recent varicella infection; and chronic lung disease (Table 1). The clinical manifestations were fever, cough, soft tissue infection, vomiting, abdominal tenderness, pharyngitis, and skin rash. The least frequent manifestations were chest pain, diarrhea, joint swelling, and altered mental status (Table 2).

Other complications were as follows: acute respiratory distress; renal impairment, localized infection in the form of pneumonia; pleural effusion, abscess, necrotizing fasciitis, septic arthritis, and osteomyelitis (Table 3).

There were 10 episodes of shock; 6 of these were pediatric patients (one case at one month of age, 2 cases at 3 months, 2 cases at 5 years, and one case at 14 years), and 4 were adult patients (aged 24 years, 43 years, 60 years, and 78 years. All of them admitted to ICU, 6 of them required inotropes and invasive respiratory support.

At the end of the period, 4 patients (12.1%) died from the illness, 27 patients (81.1%) recovered from the illness with no sequela and 2 adult patients (6.1%) recovered with sequelae, which were one patient (3%) aged 65 years showed irreversible renal failure and one patient (3%) aged 70 years (3%) had a limb loss.

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Table 1 - The underlying conditions reported in the 33 patients with Group A beta-hemolytic bacteremia.

Underlying condition	n (%)
Diabetes mellitus	6 (18.2)
Cardiac disease	11 (33.3)
Chronic lung disease	1 (3.0)
Liver disease	3 (9.0)
Immune-suppressive treatment	6 (18.2)
Malignancy	9 (27.3)
Recent trauma	6 (18.2)
Recent varicella infection	1 (3.0)
Recent influenza infection	6 (18.2)
Recent surgery or procedure	5 (15.2)
Recent antibiotic use	4 (12.1)

Table 2 - Clinical features in the 33 patients with group A beta-hemolytic bacteremia.

Features	n (%)
Fever	23 (69.7)
Vomiting	11 (33.3)
Diarrhea	4 (12.1)
Chest pain	3 (9.1)
Pharyngitis	7 (21.2)
Cough	16 (48.5)
Soft tissue infection	14 (42.4)
Skin rash	7 (21.2)
Joint swelling	3 (9.1)
Tachycardia	10 (30.3)
Hypotension	6 (18.2)
Respiratory distress	7 (21.2)
Altered mental status	3 (9.1)
Abdominal tenderness	8 (24.2)

The mortality was noted in 4 patients: occurring in 3 pediatric patients without any comorbidities (aged 3 months for one and 5 years for 2 patients) and in one adult patient, aged 78 years, with co-morbidities (liver disease, diabetes mellitus, hypertension, and congenital heart disease).

Discussion. During the past decade, there has been an increase in the number of reported cases of *Streptococcus pyogenes* bacteremia, which reflects the changing epidemiology and clinical patterns of invasive streptococcal infections especially in a population with the high proportions of intravenous drug users.^{12,13} Bacteremia in children may emanate from an upper respiratory infection, but it is more commonly associated with cutaneous foci, including burns and varicella; in

Table 3 - Complications in the 33 patients with group A beta-hemolytic bacteremia.

Complication	n (%)
Shock	10 (30.3)
Acute Respiratory Distress Syndrome	7 (21.2)
Renal impairment	7 (21.2)
Pneumonia	5 (15.2)
Pleural effusion	2 (6.1)
Abscess	3 (9.1)
Necrotizing fasciitis	3 (9.1)
Septic arthritis	1 (3.0)
Osteomyelitis	1 (3.0)

this study, only one case of varicella infection was found. In older patients, with streptococcal bacteremia as a known case of chronic illnesses, the relation of chronic illness to the bacteremia is often unclear. The low levels of protective anti-streptococcal antibodies in plasma have earlier been documented to be a predisposing factor to invasive group A streptococcal infection (IGASI). Holm et al¹⁴ suggested that the absence of specific antibodies to M-protein may predispose a patient to invasive and fatal infections. We suggest that an altered immune status of the host, as in 63% cases in our study, is also likely to be a predisposing factor for an invasive disease. These patients included diabetes mellitus (n=6), malignancy (n=9), and being on immunosuppressive medications (n=6). Malignancy (27%) and immunosuppression (18%) were the risk factors in both age groups. This study recorded 11 (33%) patients with underlying cardiac diseases, raising an interest in a recent surveillance study considering 10-year data for a population from San Francisco Bay area, USA and concluding an association between cardiac disease and IGASI.¹⁵ Nevertheless, cardiac disease increases the risk of invasive GAS disease, but the mechanism is not known and needs further investigation. Streptococcal toxin shock-like syndrome was noted in 10 patients (33%) with bacteremia. The mortality was recorded in 4 patients, which is lesser than that reported in the previous national and international studies.^{10,11,16,17} This might be attributable to the improved health care facility especially in the intensive care management.

The overall mortality in this study was found to be 12.1% and 75% in pediatric age group, but with no underlying diseases, which is lower than that recorded earlier (16-21%) in 2 previous local studies carried out in Saudi Arabia. This data is also lower than the mortality rates reported in other investigations.^{12,18,19}

Overall, our data concurred with the observed clinical presentations reported by other authors. The limitations of the study were its retrospective nature and a small sample of both adult and pediatric population.

In conclusion, Group A beta-hemolytic infection is a major health problem with high morbidity and mortality rates. This condition may present in any age group including neonates. There has been a minimal change in the disease pattern over the 28 years in Saudi Arabia. The management of the invasive GAS infection depends on accurate and timely diagnosis and an appropriate antimicrobial therapy. It is difficult to predict the outcome of the disease as the interplay between the host and the organism does not appear to contribute to its evolution. Healthy people can also acquire a GAS disease but the highest risk appears in those with any other chronic illness such as cardiac diseases, diabetes mellitus, skin diseases, and underlying malignancies. The relation of chronic illness to the bacteremia is often unclear and needs further investigation. Invasive Group A streptococcal infection still carries high mortality rate.

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