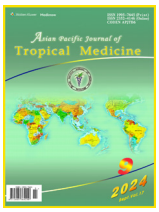

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Epidemiological observations of invasive group B *Streptococcus* infections in six major hospitals in Peninsular Malaysia

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ABSTRACT

Objective: To address the lack of research on invasive group B *Streptococcus* (GBS) infections in Malaysia and Southeast Asia through a comprehensive analysis of GBS isolates obtained from hospitals.

Methods: Medical records from patients with GBS infection isolated from the sterile site, such as blood and cerebrospinal fluid from 14 July 2019 to 15 December 2020, were reviewed from six major hospitals in Peninsular Malaysia. Inclusion criteria were invasive GBS, sterile sites and non-repeated GBS isolated from the same patients in the same admission. Viable isolates were re-identified for GBS and serotyped.

Results: A total of 118 patients were eligible, with a majority of non-pregnant adults (76.3%). Over half of the patients (62.7%) had underlying medical conditions, with diabetes as the most common disease, followed by respiratory disease, renal disease, cardiovascular disease and skin and soft tissue disease. The most common manifestations were sepsis, followed by soft tissue abscess, diabetic foot ulcer, wet gangrene and cellulitis. The overall mortality was 7.6%. The most common serotype was serotype Ⅴ.

Conclusions: Invasive GBS infection among non-pregnant adults showed a rising trend, particularly among diabetic individuals. The study underscores the importance of reducing risk factors and highlights the necessity of developing GBS vaccination as a preventive strategy for both infants and adults.

KEYWORDS: *Streptococcus agalactiae*; Group B *Streptococcus*; Invasive GBS infections; Malaysia

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Significance

This study provides an overview of the clinical manifestations of patients with invasive group B *Streptococcus* (GBS) infection and the serotype distribution of the GBS isolates in six major hospitals in Malaysia. Diabetes was the most common underlying disease associated with invasive GBS infection among non-pregnant adults, with sepsis as the most common manifestation. A majority of the GBS isolates had serotype Ⅴ. These outputs contribute to the advancement of knowledge on GBS infection-associated risk factors and serotype distribution of invasive GBS for managing the prevention and control strategy, particularly in Malaysia.

1. Introduction

Streptococcus agalactiae, or group B *Streptococcus* (GBS), is a harmless commensal bacterium that colonizes the human gastrointestinal and genitourinary tract in 15%-35% of healthy adults. Nevertheless, it is a leading cause of lethally invasive neonatal infections, such as bacteremia, pneumonia, and meningitis[1]. Additionally, it affects pregnant women and non-pregnant adults with significant comorbidities, as well as the elderly[2]. GBS infection manifests a variety of clinical manifestations. In this regard, GBS that is isolated from asymptomatic patients such as vaginal swabs, are considered colonizers. While GBS isolated from sterile sites, such as blood or cerebrospinal fluid, is regarded as an invasive isolate[3]. Globally, GBS infection has increased among pediatric and adult populations. It contributes significantly to perinatal mortality, with an estimated 147000 deaths annually, including stillbirths[4–6]. Growing populations of adults, particularly older adults, with significant underlying medical conditions such as diabetes mellitus, heart disease, and cancer, as well as obesity, may play a role in increasing invasive GBS infections[7].

In Malaysia, literary research on GBS infection in humans has identified a low number of articles since 1980s. Available studies described GBS infection and associated risk factors only at a specific location and point in time. This may not represent the real incidence of GBS infection in Malaysia, where actual cases could have not been reported. An earlier study in Malaysia reported that the GBS genital carriage rate was 9.7% in pregnant women, and the cases of GBS septicemia in neonates born in hospitals were 0.4 per 1000 live births[8]. Another study by Eskandarian *et al*.[9] reported 18 GBS bacteremia cases among neonates (5; 1 died), male adults (9; 4 died), a parturient woman (1), and non-pregnant female adults (3). GBS bacteremia was significantly associated with severe underlying diseases in neonates, pregnant women, and non-pregnant adults. A case of a six-month-old male newborn who died of sudden death owing to GBS pneumonia was recorded at Johor Bahru[10]. Moreover, another case of a 46-year-old woman with gestational diabetes mellitus who gave birth to her third child, vaginally with no complications, found dead at home after being unconscious[11]. These results raise further questions concerning the risk factors and mortality of GBS infection.

To the best of our knowledge, there is a lack of studies related to invasive GBS infections in Malaysia and Southeast Asia. Therefore, our study aimed to characterize and examine patients' clinical information with invasive GBS infection in six major Malaysian hospitals over about 1.5 years. The findings in this study will help in understanding the prevalence of invasive GBS infection in Malaysia, contributing to the advancement of knowledge on GBS infection-associated risk factors and serving as a basis for further research.

2. Subjects and methods

2.1. Study procedures and GBS isolates

This is a cross sectional and prospective study conducted in six major hospitals in Peninsular Malaysia: Hospital Tuanku Ja'afar, Seremban, Negeri Sembilan; Hospital Sultan Idris Shah, Serdang, Selangor; Hospital Sultanah Aminah, Johor Bahru, Johor; Universiti Kebangsaan Malaysia Medical Center, Cheras, Kuala Lumpur; Hospital Sungai Buloh, Sungai Buloh, Selangor and Hospital Melaka, Melaka from 14 July 2019 to 15 December 2020.

At these six hospitals, all GBS-positive cultures isolated from sterile sites (blood, cerebrospinal fluid, internal tissue, pus aspirate, peritoneal dialysis fluid, bone biopsy, skin biopsy and bone marrow) during the sample collection period were re-identified following standard microbiological methods for GBS species confirmation[12]. Restricted medical records associated with the isolates were provided by the respective participating hospitals including site of isolation, sociodemographic data (age, sex, and ethnicity), clinical manifestations, comorbidities, and mortality of patients. Repeated GBS isolated from same patients of the same admission, and non-sterile site isolates were excluded. In the case of several simultaneous invasive infections occurring in the same patient, only the most profound infection was retained. Comorbidities that were not indicated in the medical records were assumed to be nonexistent. If a death happened due to GBS infection, it was deemed a GBS-related death.

2.2. Re–identification of GBS isolates and serotyping

GBS isolates were identified by colony morphology, typical β-hemolysis showing a clear zone surrounding the colonies on 5%

Columbia sheep blood agar, catalase test and Gram stain. Wellcogen Strep B test (Oxoid, UK), Streptex Rapid Latex test (Oxoid) and CAMP test were used to confirm the results. A conventional PCR assay as described by Rosa-Fraile and Spellerberg[12] and Muthanna *et al*.[13] was used for the identification of GBS by targeting the *cfb* gene (encoding the CAMP factor). Serotype identification was carried out using multiplex PCR method according to the study by Imperi *et al*[14].

2.3. Ethical approval and data analysis

Ethical approval to conduct this study was obtained from the Medical Research and Ethics Committee of the Ministry of Health Malaysia (Approval number: NMRR 19-876-46665).

Data was statistically analyzed by Statistical Package for the Social Sciences (SPSS) software version 26.0. Descriptive statistics (frequency and percentage) were used to distribute and summarize the sociodemographic characteristics, clinical manifestations and comorbidities. For categorical data, frequencies and percentages were employed, while mean and SD were used for continuous data. Age group, sociodemographic factors, clinical manifestations, and comorbidities were analyzed using *Chi*-square test and Fisher's exact test to compare with different patient groups.

3. Results

3.1. Distribution of invasive GBS infection

After reviewing the medical records and taking the definition of invasive GBS and exclusion criteria, 118 invasive GBS infections were identified from the six major hospitals in Malaysia; 40 (33.9%) were from Hospital Sultanah Aminah, 22 (18.6%) from Hospital Sultan Idris Shah Serdang, 22 (18.6%) from Universiti Kebangsaan Malaysia Medical Center, 15 (12.7%) from Hospital Tuanku Ja'afar, 13 (11.0%) from Hospital Melaka and 6 (5.1%) from Hospital Sungai Buloh.

3.2. Characteristics of GBS isolates

Invasive GBS was mainly isolated from blood (55; 46.6%), followed by internal tissue (37; 31.4%), pus aspirate (15; 12.7%), peritoneal dialysis fluid (4; 3.4%), bone biopsy (3; 2.5%), cerebrospinal fluid (2; 1.7%), skin biopsy (1; 0.8%) and bone marrow (1; 0.8%). Five GBS isolates retrieved from the 118 invasive GBS cases did not survive, therefore 113 GBS isolates were used for serotyping and other analysis.

Phenotypic characteristics of the GBS isolates were confirmed where GBS produced a zone of β hemolytic around the colonies on the blood agar, following 24 hours of incubation under anaerobic conditions. Positive CAMP results were indicated by an arrowhead GBS β-hemolytic zone perpendicular to *Staphylococcus aureus*, a Gram-positive coccus with a tendency to form chains, negative catalase result for GBS isolates and positive result of GBS using a Latex agglutination. Additionally, all the GBS isolates were tested positive for *cfb* gene by PCR analysis.

3.3. Clinical manifestations of patients with invasive GBS

The characteristics of the 118 patients were reported in Table 1.

Table 1. Characteristics of patients with invasive group B *Streptococcus* infections per age group [*n* (%)].

Variables	Total cases (*n*=118)	Neonate and infant (*n*=17)	15-<40 years (*n*=26)	⩾40-<65 years (*n*=60)	⩾65 years (*n*=15)	*P* value
Sex						
Male	45 (38.1)	4 (23.5)	7 (26.9)	28 (46.7)	6 (40.0)	0.111
Female	73 (61.9)	13 (76.5)	19 (73.1)	32 (53.3)	9 (60.0)	
Ethnicity						
Malay	85 (72.0)	13 (76.5)	18 (69.2)	46 (76.7)	8 (53.3)	
Indian	16 (13.6)	3 (17.6)	3 (11.5)	5 (8.3)	5 (33.3)	0.503[a]
Chinese	17 (14.4)	1 (5.9)	5 (19.2)	9 (15.0)	2 (13.3)	
Status						
Non-pregnant adults	90 (76.3)	0 (0.0)	17 (65.4)	58 (96.7)	15 (100.0)	
Pregnant women	11 (9.3)	0 (0.0)	9 (34.6)	2 (3.3)	0 (0.0)	<0.001[a]
Neonate and infant	17 (14.4)	17 (100.0)	0 (0.0)	0 (0.0)	0 (0.0)	
Underlying condition						
⩾1 underlying condition	74 (62.7)	0 (0.0)	10 (38.5)	52 (86.7)	12 (80.0)	<0.001[a]
Diabetes mellitus	57 (48.3)	0 (0.0)	9 (34.6)	41 (68.3)	7 (46.7)	<0.001[a]
Renal disease	6 (5.1)	0 (0.0)	0 (0.0)	5 (8.3)	1 (6.7)	0.138[a]
Neurologic disease	3 (2.5)	0 (0.0)	0 (0.0)	2 (3.3)	1 (6.7)	0.196[a]
Cardiovascular disease	4 (3.4)	0 (0.0)	1 (3.8)	2 (3.3)	1 (6.7)	0.368[a]
Respiratory disease	8 (6.8)	2 (11.8)	2 (7.7)	1 (1.7)	3 (20.0)	1.000[a]
Skin and soft tissue disease	4 (3.4)	0 (0.0)	1 (3.8)	3 (5.0)	0 (0.0)	0.684[a]
Autoimmune disease	2 (1.7)	0 (0.0)	2 (7.7)	0 (0.0)	0 (0.0)	0.533[a]
Cancer and tumor	1 (0.8)	0 (0.0)	1 (3.8)	0 (0.0)	0 (0.0)	0.657[a]
Gastroenteritis	1 (0.8)	0 (0.0)	0 (0.0)	1 (1.7)	0 (0.0)	0.657[a]
Death	9 (7.6)	6 (35.3)	1 (3.8)	2 (3.3)	0 (0.0)	0.002[a]

[a]Fisher's exact test, otherwise *Chi* square test was used.

Patients were predominantly female (61.9%), with a mean (SD) age of 42.3 (22.6) years old. Most of the patients were non-pregnant adults (90; 76.3%), followed by neonate (17; 14.4%) and pregnant women (11; 9.3%). One or more underlying conditions were found in 74 (62.7%) of the cases. The most common underlying conditions were diabetes mellitus (48.3%), respiratory disease (6.8%), renal disease (5.1%), cardiovascular disease (3.4%), skin and soft tissue disease (3.4%) and neurologic disease (2.5%). Diabetes mellitus was more common in patients ⩾40-<65 years of age than in younger age groups. The overall mortality was 7.6%, with neonates and congenital pneumonia.

Sepsis, soft tissue abscess, diabetic foot ulcer, wet gangrene, cellulitis, and congenital pneumonia and puerperal sepsis were the most frequent clinical manifestations of invasive GBS infection.

Table 2. Clinical manifestations of patients with invasive group B *Streptococcus* infections [*n* (%)].

Variables	Total cases (*n*=118)	Neonate and infant (*n*=17)	15-<40 years (*n*=26)	⩾40-<65 years (*n*=60)	⩾65 years (*n*=15)	*P* value
Sepsis	25 (21.2)	10 (58.8)	5 (19.2)	7 (11.7)	3 (20.0)	<0.001
Soft tissue abscess	15 (12.7)	0 (0.0)	3 (11.5)	10 (16.7)	2 (13.3)	0.112[a]
Diabetic foot ulcer (DFU)	13 (11.0)	0 (0.0)	0 (0.0)	11 (18.3)	2 (13.3)	0.027[a]
Wet gangrene	8 (6.8)	0 (0.0)	2 (7.7)	6 (10.0)	0 (0.0)	0.517[a]
Cellulitis	7 (5.9)	0 (0.0)	0 (0.0)	6 (10.0)	1 (6.7)	0.121[a]
Congenital pneumonia	5 (4.2)	4 (23.5)	0 (0.0)	0 (0.0)	1 (6.7)	0.001[a]
Puerperal sepsis	5 (4.2)	0 (0.0)	4 (15.4)	1 (1.7)	0 (0.0)	0.544[a]
Peritonitis	4 (3.4)	0 (0.0)	0 (0.0)	3 (5.0)	1 (6.7)	0.177[a]
Necrotizing fasciitis	4 (3.4)	0 (0.0)	2 (7.7)	2 (3.3)	0 (0.0)	1.000[a]
Pneumonia	4 (3.4)	0 (0.0)	0 (0.0)	1 (1.7)	3 (20.0)	0.024[a]
Tenosynovitis	3 (2.5)	0 (0.0)	0 (0.0)	3 (5.0)	0 (0.0)	0.438[a]
Septic arthritis	3 (2.5)	0 (0.0)	1 (3.8)	2 (3.3)	0 (0.0)	0.796[a]
Scrotal abscess	2 (1.7)	0 (0.0)	1 (3.8)	1 (1.7)	0 (0.0)	1.000[a]
Chorioamnionitis	2 (1.7)	0 (0.0)	2 (7.7)	0 (0.0)	0 (0.0)	0.528[a]
Osteomyelitis	2 (1.7)	0 (0.0)	2 (7.7)	0 (0.0)	0 (0.0)	0.528[a]
Meningitis	2 (1.7)	2 (11.8)	0 (0.0)	0 (0.0)	0 (0.0)	0.012[a]
Postpartum hemorrhage	2 (1.7)	0 (0.0)	1 (3.8)	1 (1.7)	0 (0.0)	1.000[a]
Acute pulmonary oedema	2 (1.7)	1 (5.9)	0 (0.0)	1 (1.7)	0 (0.0)	0.528[a]
Other[*]	9 (7.6)	0 (0.0)	2 (7.7)	5 (8.3)	2 (13.3)	0.300[a]

[*]Other clinical syndrome included frontotemporal dementia, mitral valve stenosis, large subchorionic hematoma, pyelonephritis, acute gastroenteritis, cardiogenic shock syndrome, endocarditis, end stage of renal disease (ESRD) and meningoencephalitis. [a]Fisher's exact test, otherwise *Chi* square test was used.

Table 3. Serotype distribution of invasive group B *Streptococcus* isolates in relation to patient age group.

Age group	[*]Serotypes, *n* (%)									*P* value
	Ⅰa	Ⅰb	Ⅱ	Ⅲ	Ⅳ	Ⅴ	Ⅵ	Ⅶ	Ⅸ	
Neonate and infant (*n*=16)	2 (12.5)	1 (6.3)	0 (0.0)	6 (37.5)	1 (6.3)	1 (6.3)	3 (18.8)	2 (12.5)	0 (0.0)	0.004[a]
15-<40 years (*n*=25)	3 (12.0)	1 (4.0)	5 (20.0)	1 (4.0)	1 (4.0)	10 (40.0)	3 (12.0)	0 (0.0)	1 (4.0)	0.287[a]
⩾40-<65 years (*n*=57)	16 (28.1)	2 (3.5)	12 (21.1)	2 (3.5)	1 (1.8)	14 (24.6)	7 (12.3)	3 (5.3)	0 (0.0)	0.067[a]
⩾65 years (*n*=15)	1 (6.7)	0 (0.0)	4 (26.7)	3 (20.0)	1 (6.7)	1 (6.7)	5 (33.3)	0 (0.0)	0 (0.0)	0.508[a]

[*]Serotypes and analysis were based on 113 viable isolates. [a]Fisher's exact test was used.

Table 4. Serotype distribution of invasive group B *Streptococcus* isolates in relation to clinical manifestations.

Clinical manifestations	[**]Serotype, *n* (%)									*P* value
	Ⅰa	Ⅰb	Ⅱ	Ⅲ	Ⅳ	Ⅴ	Ⅵ	Ⅶ	Ⅸ	
Sepsis (*n*=24)	3 (12.5)	1 (4.2)	1 (4.2)	4 (16.7)	3 (12.5)	5 (20.8)	5 (20.8)	2 (8.3)	0 (0.0)	0.131[a]
Soft tissue abscess (*n*=14)	2 (14.3)	0 (0.0)	5 (35.7)	0 (0.0)	1 (7.1)	4 (28.6)	2 (14.3)	0 (0.0)	0 (0.0)	0.859[a]
Diabetes mellitus (*n*=55)	14 (25.5)	2 (3.6)	10 (18.2)	2 (3.6)	2 (3.6)	17 (30.9)	6 (10.9)	2 (3.6)	0 (0.0)	0.259
Diabetic foot ulcer (DFU) (*n*=11)	2 (18.2)	0 (0.0)	2 (18.2)	1 (9.1)	0 (0.0)	3 (27.3)	3 (27.3)	0 (0.0)	0 (0.0)	0.681[a]
Wet gangrene (*n*=8)	4 (50.0)	0 (0.0)	1 (12.5)	0 (0.0)	0 (0.0)	3 (37.5)	0 (0.0)	0 (0.0)	0 (0.0)	0.118[a]
Cellulitis (*n*=7)	2 (28.6)	1 (14.3)	0 (0.0)	1 (14.3)	0 (0.0)	2 (28.6)	1 (14.3)	0 (0.0)	0 (0.0)	0.553[a]
Congenital pneumonia (*n*=5)	0 (0.0)	0 (0.0)	0 (0.0)	2 (40.0)	0 (0.0)	1 (20.0)	1 (20.0)	1 (20.0)	0 (0.0)	0.158[a]
Puerperal sepsis (*n*=4)	1 (25.0)	0 (0.0)	1 (25.0)	0 (0.0)	0 (0.0)	2 (0.0)	0 (50.0)	0 (0.0)	0 (0.0)	0.751[a]
Peritonitis (*n*=4)	0 (0.0)	0 (0.0)	2 (50.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (50.0)	0 (0.0)	0 (0.0)	0.577[a]
Necrotizing fasciitis (*n*=4)	0 (0.0)	0 (0.0)	1 (25.0)	0 (0.0)	0 (0.0)	2 (50.0)	0 (0.0)	1 (25.0)	0 (0.0)	0.225[a]
Pneumonia (*n*=4)	0 (0.0)	0 (0.0)	0 (0.0)	1 (25.0)	0 (0.0)	1 (25.0)	2 (50.0)	0 (0.0)	0 (0.0)	0.152[a]
Other[*] (*n*=27)	8 (29.6)	2 (7.4)	7 (25.9)	3 (11.1)	0 (0.0)	3 (11.1)	2 (7.4)	1 (3.7)	1 (3.7)	0.123[a]
Death (*n*=9)	1 (11.1)	0 (0.0)	1 (11.1)	2 (22.2)	0 (0.0)	1 (11.1)	2 (22.2)	1 (11.1)	1 (11.1)	0.109[a]

[*]Other clinical syndrome included tenosynovitis, septic arthritis, scrotal abscess, chorioamnionitis, osteomyelitis, meningitis, postpartum hemorrhage, acute pulmonary oedema, frontotemporal dementia, mitral valve stenosis, large subchorionic hematoma, pyelonephritis, acute gastroenteritis, cardiogenic shock syndrome, endocarditis, end stage of renal disease (ESRD) and meningoencephalitis. [**]Serotypes and analysis were based on 113 viable isolates. [a]Fisher's exact test, otherwise *Chi* square test was used.

Patients aged 65 and older were more likely to have pneumonia. In contrast, patients aged ⩾40-<65 were more likely to have soft tissue abscess, diabetic foot ulcers, wet gangrene, and cellulitis. Also, sepsis, congenital pneumonia and meningitis were more common in neonates and infants (Table 2).

3.4. Serotype distribution of invasive GBS

The serotype distribution of the GBS strains is presented in Figure 1 based on the number of viable isolates (n=113). The most common serotype was serotype Ⅴ (n=26; 23.0%), followed by Ⅰa (n=22; 19.5%), Ⅱ (n=21; 18.6%), Ⅵ (n=18; 15.9%), Ⅲ (n=12; 10.6%), Ⅶ (n=5; 4.4%), Ⅰb and Ⅳ, (n=4; 3.5% each) and Ⅸ (n=1; 0.9%), while serotype Ⅷ was not found.

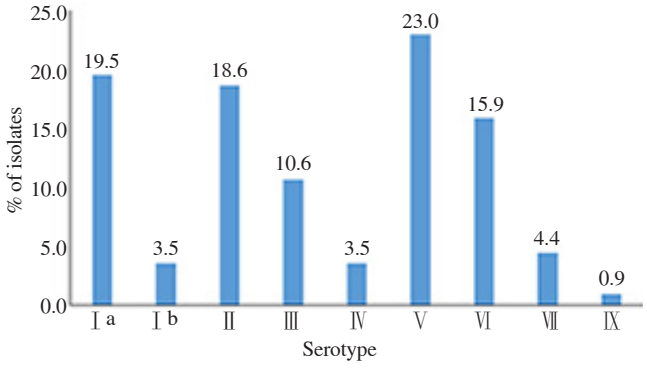

Figure 1. Serotype distribution of invasive group B *Streptococcus* isolates.

Serotype distributions (n=113) varied according to the patients' age group (Table 3). There was a significant association between serotypes and, neonate and infant (P=0.004), while there was no significant association between serotypes and other age groups. In addition, serotype distribution among GBS isolates differed based on clinical manifestations without significant association (Table 4).

4. Discussion

We conducted a cross sectional and retrospective study in six major hospitals in Peninsular Malaysia to evaluate the incidence, clinical manifestations, characteristics and outcomes of invasive GBS infection in patients in Malaysia. Invasive GBS infection is defined as the isolation of GBS from normal sterile sites such as blood, cerebrospinal fluid and internal tissue in patients.

The estimated burden of GBS infections in developing countries remains to be determined. In a meta-analysis, the worldwide incidence of GBS infection was estimated to be 0.53 per 1000 live births, with a mean case-fatality rate of 9.6%; however, only few studies from Southeast Asia were included[15]. Another meta-analysis estimated that the prevalence of rectovaginal GBS among women was 17.9% with the lowest prevalence in Southeast Asia (11.1%)[16]. A study conducted in Malaysia reported that the GBS vaginal rate among pregnant women was 9.7%, with GBS annual incidence in children of 0.4 per 1000 live births[17].

In our study, we found 118 cases of invasive GBS occurred in 90 non-pregnant individuals, 16 neonates, 11 pregnant women, and one infant. Females accounted for more than 60% of the cases, corroborating the findings of prior studies on sex distribution[18,19]. The presence of GBS as normal flora in the genitourinary tract in women might explain female dominance[1]. Invasive GBS infection manifests including sepsis, soft tissue abscesses, diabetic foot ulcers, wet gangrene and cellulitis in more than half of the cases. Similar to previous studies, sepsis, soft tissue abscesses, and diabetic foot ulcers were shown to be typical clinical manifestations of invasive GBS infection[20-23].

In this study, more than 60% of patients have an underlying disease, the most frequent of which is diabetes mellitus. In addition, renal disease, neurologic disease, cardiovascular disease, respiratory disease, skin and soft tissue disease, autoimmune disease, cancer and tumour, and gastroenteritis, were reported. Our findings are consistent with studies in Europe, the United States[24-26] and previous limited studies in Malaysia[9,23] where diabetes was the most common risk factor for invasive GBS infections. Cancer and tumours were less prevalent, which were similar with previous results in Malaysia[9] and France[24] but different from European countries[20,26].

The overall mortality rate in this study was 7.6%, which included six neonatal cases and three adult cases. We found that the case mortality rate was lower than prior findings, which ranged from 9% to 20%[20-22,27]. Other studies reported the global mortality for patients with invasive GBS estimated to be between 3.0% and 8.1%[28,29]. In this study, higher mortality was associated with neonates and congenital pneumonia; this is inconsistent with previous studies[21,27]. Moreover, cancer, sepsis, peritonitis, endocarditis, and meningitis were also associated with mortality among GBS infections[30,31].

In general, there has been an increase in prevalence of invasive GBS infections in Malaysia compared to prior studies[9,32]. Invasive GBS infection has become more common in many countries, and it has been associated with higher mortality rates over time[6,25,28,33,34]. An ageing population, as well as increased obesity and diabetes rates, might be attributed to this rise in invasive GBS infections[34-36].

Meanwhile, previous studies in Malaysia have shown that serotypes Ⅴ and Ⅰa are the most common serotypes among human invasive GBS isolates from sterile isolation sites associated with mortality[23,37]. As a result, serotype Ⅴ can be regarded as one of the most widespread serotypes among human isolates in Malaysia from

2009 to date[23,37,38].

In another study in Malaysia, the most common serotype from sterile and non-sterile isolation sites was Ⅴ, followed by Ⅶ, Ⅲ, Ⅰa and Ⅴ[39]. A study in Taiwan reported that serotype Ⅲ and Ⅰa are the most frequently identified serotypes responsible for invasive diseases in neonates, while type Ⅵ, Ⅰb and Ⅴ are associated with invasive diseases in adults[40]. According to a study of infants and children, serotype Ⅰa was the most prevalent among infants less than 72 hours old, whereas serotype Ⅲ was predominant among older infants. The study found that serotype Ⅰa-patients were significantly younger, had more perinatal maternal fever, and had higher mortality compared to serotype Ⅲ-patients[41]. According to a study in Japan, serotypes Ⅲ and Ⅰb are much more common in both neonates and adults[42].

In Malaysia, invasive GBS among non-pregnant adults indicates a growing burden, especially among the elderly and those with chronic illnesses, such as diabetes. Furthermore, GBS have also been observed to cause a large number of non-invasive infections[43]; thus, the overall impact is likely to be higher. Reducing risk factors by controlling the underlying diseases may assist in preventing invasive GBS infections. In addition, developing a GBS vaccination is likely to be necessary as a preventive strategy for both infants and adults. Future research is needed to determine the vaccine's potential influence on invasive GBS infections.

Conflict of interest statement

The authors report no conflict of interest.

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Availability of data and materials

The datasets that are used and/or analysed in this study can be made available upon reasonable request.

Authors' contributions

AM and MNMD contributed to both data curation and investigation. NAA, CHA, ZI, LAMN, MMA and NHA contributed to the sample collection. AM, NAA, NDD and NHZB contributed to the methodology. AM contributed to writing the original draft. MNMD, MNAA and SAN contributed to writing, reviewing, and editing the manuscript. AM, MNMD and NAA contributed to data analysis. MNMD, MNAA and SAN were involved in project administration and supervision.

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