

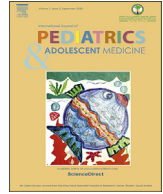
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Original research article

Incidence and outcome of group B streptococcal invasive disease in Omani infants



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ABSTRACT

Objectives: Group B streptococcus (GBS) infection is a serious disease that continues to cause high morbidity and mortality. It is one of the leading cause of sepsis; particularly meningitis, in infants and young children all around the world. In this study, we aim to identify the incidence of GBS sepsis in Omani infants less than 3 months of age who were born at Royal Hospital and who presented with clinical sepsis and positive culture. In addition, we aim to describe the clinical presentation and complications noted on admission and then on follow-up visit.

Methods: This is an observational retrospective chart review study. It included all Omani infants (0–3 months) who were diagnosed to have GBS sepsis/meningitis from 2006 to 2016 at the Royal Hospital, Muscat, Sultanate of Oman.

Results: There were 83,000 live births in the Royal Hospital over a period of 10 years. Thirty-eight babies had culture proven GBS infection, with an overall incidence rate of neonatal GBS of 0.46 per 1000 live births with 95% confidence intervals. There were no significant variations in the annual rates of infection during the study period, ranging from around 1–7 cases per year. Additional 5 cases of GBS sepsis presented to Royal Hospital are either through Emergency Department or as referrals from other hospitals, giving us a total of 43 cases of proven GBS infections. Out of the 43 cases, 8 were born prematurely (19%), either before (<34 weeks, n = 2) or during (34–36 weeks, n = 6). Term babies were 35 out of 43 with percentage of 81% of the total. Three died, resulting in a case mortality of 7.0%.

Conclusion: Our GBS incidence is comparable to that of screened population internationally. At the time being, with the best available results, maternal screening might not seem cost effective in our current settings. A cost effective study is required before implemented a national screening programme in the Country. However, this research will definitely help in the process of any future plans of implantation of new guidelines, as it can be used as leading point for future prospective studies.

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1. Introduction

Group B streptococcus is one of the leading cause of sepsis in young infants, followed by *E. coli* infection. Outcome from GBS infection can be devastating if left untreated. It is estimated to be responsible for more than 40% of all early-onset infections in neonates [1].

GBS infection in neonates is divided into 3 categories: early onset GBS disease (from 0 to 6 days of life), late onset GBS (7–90

days) and very late onset GBS (>90 days). Chances of having GBS infection decrease with age, becoming very unlikely after the age of three months [2,3].

In the UK, early onset GBS sepsis account for more than two third of the cases of neonatal sepsis, with a rate of 0.57 per 1,000 live births in 2014.(3) Early onset sepsis is usually apparent during or soon after delivery in the form of respiratory distress and pneumonia. 90% of infected infants manifested within the first 24 h of life [1]. Most of them present with symptoms that include: temperature instability, grunting and abnormal breathing, poor feeding and lethargy.

Late onset sepsis occurs after the first 6 days of life, usually in form of meningitis and bacteraemia. Clinical presentation in late onset sepsis can be very similar to those of early onset sepsis.

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Further symptoms may include bulging fontanelle, abnormal body movement and stiffness, septic arthritis and osteomyelitis. In the UK, late onset GBS sepsis (LOGBS) was estimated to account for 0.37 per 1,000 live births in 2014 [2].

In 2015, the US rate for early onset GBS sepsis (EOGBS) was 0.23 per 1000 live births and for LOGBS 0.34 per 1000 live births [4].

A recent paper published in the International Journal of Infectious Disease, published on Feb 2017, looked at the culture proven early onset neonatal sepsis in Arab states in the Gulf region including Saudi Arabia, Kuwait and the United Arab Emirates. Results showed that the overall incidence of GBS disease was 0.9 per 1000 live births, ranging from as high as 1.4 per 1000 in Kuwait to 0.6 per 1000 in Dubai [5].

Pediatricians usually rely on clinical picture of sepsis and a positive blood, CSF or other relevant culture to support their clinical diagnosis. Unfortunately, in majority of cases lumbar puncture is deferred due to instability of the neonates, and when obtained, the results of the cultures may be compromised or altered by the use of antibiotics. Newer tests like polymerase chain reaction (PCR) are promising and may help in the early and accurate diagnosis of GBS sepsis.

Multiple clinical trials conducted in the 1980s showed that the use of intrapartum antibiotic prophylaxis (IAP) was an effective means of reducing the incidence of early onset GBS infection by interrupting the vertical transmission between colonized mothers and their babies [6,7]. However, the use of IAP was only adopted in 1996 and in 2002 the universal antenatal screening for GBS colonization was announced by The American College of Obstetricians and Gynecologists (ACOG) along with the American Academy of Pediatrics (AAP). This screening is done through culturing of all pregnant women for rectovaginal GBS colonization at 35–37 weeks of gestation, with subsequent use of intrapartum antibiotic prophylaxis for GBS carriers. Since then, the incidence of early-onset GBS infections has decreased significantly from (1.8 cases per 1000 live births in 1990 to 0.26 cases per 1000 live births in 2010) [8]. Another comparison study in the U.S was done to compare the period between 2003 and 2005, to that just before the implantation of screening program, 2000–2001. Results showed significant reduction of 33% in the incidence of early onset neonatal sepsis. However, the incidence of late-onset GBS disease remained unchanged [1,6].

1.1. Rational and justification of the research

Since universal maternal screening is not yet the standard of care in governmental hospitals in Oman, we aimed to assess the magnitude of the problem and to identify the incidence of GBS infection, mortality and morbidity and then to compare it internationally.

1.2. Objectives

1.2.1. Primary

To identify the incidence of GBS sepsis in Omani infants less than 3 months of age, who were born at the Royal Hospital (RH).

1.2.2. Secondary

To describe the clinical presentations and outcome of infants with GBS sepsis who are admitted at the Royal Hospital.

2. Methodology

This is a retrospective chart review study that was conducted in Royal Hospital, Muscat, Oman.

Target population was Omani infants (0–3 months) who were

diagnosed to have GBS sepsis/meningitis from 2006 to 2016. This study included Omani infants (0–3 months) who were diagnosed with positive blood, CSF, urine or umbilical swab of GBS culture (whether born initially at RH or referred to it from all around the country) with signs and symptoms of clinical sepsis. Any non-Omani patients, age above 3 months and those with suspected/presumed infection (without proven cultures) were excluded from the study.

This study was approved by the ethical and research committee at the RH. Sample was collected through tracing of blood/CSF/urine and umbilical swab cultures through microbiology department. Clinical data of the patients were then collected from Al Shifa System. Consent was not applicable as this is retrospective study that looked back into data obtained from electronic data base AL Shifa over 10 years period.

Data collection includes: Demographic data of the patients like age at presentation, gender and area of residence. It also included clinical presentation, laboratory finding, management and follow-up information. The software SPSS used to calculate the outcome parameters and *P* value of less than 0.05 was taken as significant.

3. Results

There were 83,000 live births in the RH over a period of 10 years from 1 January 2006 to 30 October 2016. Out of these, only 38 babies had culture proven GBS infection, with an overall incidence rate of neonatal GBS of 0.46 per 1000 live births with 95% confidence intervals. There were no significant variations in the annual rates of infection during the study period, ranging from around 1–7 cases per year.

Additional 5 cases of GBS sepsis presented to RH care either through Emergency Department or referrals from other Hospitals, giving a total of 43 cases of proven GBS infections.

Out of the 43 cases, 8 were born prematurely (19%), either before (<34 weeks, *n* = 2) or during (34–36 weeks, *n* = 6). Term babies were 35 out of 43 with percentage of 81% of the total.

Results showed that 28 cases of EOGBS, out of which, 20 cases (75%) presented within the first 24 h following birth. Of the remaining cases, four (14.2%) were diagnosed by 48 h and two (7.1%) by 72 h. No infant with EOGBS was diagnosed between 72 h and 5 days following delivery. However, we had 2 cases who presented on day 6 of life.

Respiratory distress was the most common presentation of EOGBS infection, occurring in 21 of the total 28 infants (75%). None of the late onset GBS sepsis (LOGBS) babies had respiratory compromise (*P* = .0001). Majority of the LOGBS presented with fever, lethargy and poor feeding (80%, *P* = .0010). Complication of seizure was noted in both groups (2 in each). The clinical signs of infection are shown in Table 1.

Bacteremia, with or without an additional focus was the most common manifestation, mostly occurring in babies less than 6 days of age. Twenty four positive blood cultures were reported in early neonatal sepsis compared to only 11 in late neonatal sepsis. We had 3 positive CSF cultures in early sepsis compared to 4 in late neonatal sepsis. Four babies had positive umbilical GBS culture, with one of them progressing to necrotizing fasciitis and septic shock. No positive urine cultures noted in both groups.

Of the 43 infants, 3 died, resulting in a case mortality of 7.0%. Two of the deaths occurred in preterm babies (33 and 35 weeks of gestation). Both preterm infants who died of GBS infection developed respiratory distress within first 24 h of life. The third death occurred in a term baby who presented on day 6 of life with fever, poor feeding and seizures. Septic workup revealed positive GBS culture from umbilical discharge. Blood culture was negative as he was already on antibiotics coverage from other Hospital, while CSF

Table 1
Clinical presentations in relation to onset of disease. Oman, 2008–2016.

Variable	Age of Presentation		P value
	1–6 days	7–89 days	
	n (%)	n (%)	
Respiratory distress			
Yes	21 (75.0)	0 (0)	0.0001*
No	7 (25.0)	15 (100.0)	
Fever			
Yes	5 (17.9)	12 (80.0)	0.0001*
No	23 (82.1)	3 (20.0)	
Lethargy			
Yes	3 (10.7)	10 (66.7)	0.0001*
No	25 (89.3)	5 (33.3)	
Poor feeding			
Yes	4 (14.3)	9 (60.0)	0.004*
No	24 (85.7)	6 (40.0)	
Seizure			
Yes	2 (7.1)	2 (13.3)	0.602
No	26 (92.9)	13 (86.7)	

was not done. The baby progressed to necrotizing fasciitis and died in less than 24 h after presentation.

Since the study was conducted in a hospital with no screening policy, only five mothers had their GBS swab taken before delivery. Some of these were mothers who presented with vaginal discharges during their antenatal visits.

Mothers who had a history of vaginal discharge and positive vaginal swab culture did not receive intrapartum intravenous antibiotics. Mothers with prolonged rupture of membrane more than 18 h, were screened and prophylactically treated before results were traced.

4. Discussion

Group B streptococcus (*Streptococcus agalactiae*) is an encapsulated gram positive diplococcus that colonizes the gastrointestinal tract and genital tract of 15–40% of pregnant women. Although GBS colonization is usually asymptomatic it is still a leading risk factor for neonatal infection in infants less than 3 months of age [9]. The maternal neonatal transmission generally occurs after the onset of labour or after rupture of foetal membranes. However, vertical transmission can also occur during pregnancy as GBS can cross even intact membrane, causing preterm labour and premature rupture of membrane. It is also recognised as a rare possible cause of still birth [2].

Neonatal GBS infection is recognised as a major health issue a long time back. An old paper published in Belgium in 1979 studied the effect of GBS colonization in 1,115 pregnant women in their last trimester. Study showed that almost 6.82% women had GBS colonization, out of which majority were first time pregnant mothers. Twenty-nine out of 68 (42.6%) infants born to GBS positive mothers were found to be colonized at birth [2].

Our results findings were consistent with that described internationally. Early onset GBS sepsis (EOGBS) occurs more commonly in term infants. The main presentation was respiratory symptoms within the first 24 h of birth, and it is usually associated with bacteremia with or without pneumonia [7].

The noted complication during admission were mainly of respiratory compromise (consisting of hypoxia, respiratory distress and need for respiratory support), accounting for 18% of all complications, followed by seizures (16%) then septic shock (9%) and death (7%).

Despite the fact that mortality rate is coming down, GBS infection continues to cause significant morbidity in its survivors. A

recent study published on March 2012, further strengthened this fact. They identified 90 infants who were diagnosed with GBS meningitis from 1998 through 2006 from 2 major children's hospitals. Result showed that 5 infants died acutely after presentation, 5 died at 6 months to 3 years of age, and only 43 survivors were able to be consented to be enrolled in the study. In their study, results showed that 56% children evaluated demonstrated age-appropriate development, 25% had mild-to-moderate impairment, and 19% had severe impairment [10].

Patients with GBS bacteremia and smooth recovery course were not followed up; only those with proven CSF cultures or complicated disease during admission were followed as outpatients. Two neonates had mild seizures well controlled on medications, two had spasticity and one had mild development delay.

All 43 newborns received appropriate antibiotic treatment for GBS infection. Antibiotics received were either cefotaxime or Ampicillin and Gentamycin for 10–14 days. Those with positive CSF culture received prolonged antibiotics course of 3 weeks.

Although term infants accounted for 35 of the 43 cases of GBS sepsis, only one death occurred in this group, compared to 2 in preterm babies. This difference in mortality is consistent with previous studies.

5. Limitations

The limitations of this study includes: lack of proper documentation of old records and lack of proper follow up of mothers swabs culture results.

We also noted that follow-up visit lacked standardized neurological assessments tools, and therefore we only relied on individual subjective assessments of the examiners.

In addition, some of the patients were referred back to their local Hospitals and did not present to RH for their follow-up.

CSF studies were not obtained for all patients with GBS sepsis. In addition, data on culture-proven GBS infection are likely to underestimate the true burden of GBS because of false-negative blood or CSF culture.

6. Conclusions

The result of our study demonstrated that the incidence of GBS sepsis in Omani children born at the RH was found to be similar to that of international level of screened population although our data lack concurrent control. We noticed that even mothers who had their high vaginal swab culture taken secondary to vaginal discharges, failed to receive antibiotics due to lack of proper follow-up of the results. Therefore, maternal screening in our current setting might not be cost effective as the incidence of GBS is low. A well-structured prospective study is required before a screening programme can be implemented in the Country. However, this research will definitely help in the process of any future plans of implantation of new guidelines, as it can be used as leading point for future prospective studies.

7. Advances in knowledge

This paper aims to identify the incidence of GBS sepsis in Omani infants less than 3 months of age born at the Royal Hospital as there is no previous local data available in regard to this clinical entity.

8. Application to patient care

The result of this study showed that the routine GBS screening may not be cost effective as the incidence is low and is comparable to international incidence post GBS screening program.

Conflicts of interest

All three authors have no conflict of interest to disclose.

Ethical statement

The ethical approval for this research was obtained from the research and ethical committee at the Royal Hospital, Muscat, Oman.

Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.ijpam.2019.05.002>.

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