

Group B Streptococcus: Maternal Carriage Rate and Early Neonatal Septicaemia

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Abstract

Between January 1984 and December 1994, 30 cases of early neonatal group B streptococcus (GBS) septicaemia were managed in the Neonatal Unit, University Hospital, Kuala Lumpur. Two neonates were outborn and 28 were inborn, giving an average annual incidence of neonatal GBS septicaemia of 0.4/1000 livebirths among inborn babies. In a separate survey over a three-month period, GBS genital carriage rate among 196 parturients was found to be 9.7%.

Of the infants with GBS septicaemia, the mean gestational age was 37.5 ± 3.8 weeks and the mean birthweight was 2540 ± 716 g. Twelve (40%) were preterm infants and 14 (47%) were low birthweight infants. Male and female infants were almost equally affected. Prolonged rupture of membranes and maternal pyrexia accounted for only 5 (17%) and 3 (10%) of the cases respectively. Twenty-four (80%) neonates had onset of symptoms within 6 hours of life and respiratory symptoms were observed in 24 (80%) of the cases, while meningitis was uncommon.

Six (20%) neonates died. Preterm and low birthweight infants had higher mortality than their term counterparts: 42% versus 6% and 36% versus 6% respectively. Of those who died, 4 (67%) required respiratory support right from birth and the mean time of onset of symptoms was 4 hours (range 0 to 21 hours) and the duration of survival was only 28.8 hours (range 12 to 38 hours). As the incidence of neonatal GBS septicaemia was low, mass screening and chemoprophylaxis for GBS were not recommended. All the GBS isolates were sensitive to penicillin and ampicillin, thus one of these antibiotics should be included in the antimicrobial therapy of septic neonates.

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Key words: Antibiotic susceptibility, Clinical presentation, Risk factors

Introduction

Early neonatal infection due to Group B beta-haemolytic streptococcus (GBS or *Streptococcus agalactiae*) was first described in 1958 by Nyhan and Fousek.¹ Since its emergence as a pathogen in neonates in the seventies, it remains a major cause of neonatal morbidity and mortality of infective origin.² The epidemiology of GBS in parturient mothers and neonates has been extensively studied in the United States and Europe, but not in Malaysia. Indeed the maternal genital carriage rate of GBS and neonatal septicaemia caused by GBS are thought to be low in Malaysia.

The aims of this paper were:

- (i) to report the incidence of maternal carriage of GBS,
- (ii) to show the annual incidence of neonatal GBS septicaemia, and
- (iii) to report clinical aspects of neonatal GBS septicaemia.

Materials and Methods

Vaginal GBS Carriage Rate Among Parturient Females

Over a 3-month period, parturient females who were admitted to the labour ward of University Hospital, Kuala Lumpur were randomly selected and a high vaginal swab was taken before a vaginal examination was performed. The samples were then sent to the laboratory of the Department of Medical Microbiology and cultured in Todd-Hewitt broth. Subcultures were made on to blood agar and streptococcal colonies were identified as GBS with specific antisera (Streptex, Wellcome, UK). However, the serotypes of the isolates and the sensitivity pattern were not studied.

Neonatal Disease: Early GBS Septicaemia

Medical records of neonates who had GBS isolated from the blood were reviewed in detail with respect to

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obstetric history, clinical presentation, laboratory, radiological, and microbiological findings, and treatment. In addition, the records of neonatal blood cultures done in the Department of Medical Microbiology from 1984 to 1994 were reviewed and patients with positive GBS cultures from the blood were identified and their case records retrieved and studied in detail.

The diagnostic criteria of early GBS septicaemia were:

1. the presence of clinical features e.g. poor feeding, lethargy, temperature instability, fever, hypothermia and skin mottling within the first week of life;
2. the presence of supportive laboratory findings e.g. anaemia, thrombocytopenia, leukocytosis, leukopenia, metabolic acidosis disseminated intravascular coagulopathy and radiological findings of pneumonia.

Meningitis was diagnosed when there was a positive culture for GBS in the cerebrospinal fluid (CSF) accompanied by biochemical changes in the CSF and clinical symptoms and signs consistent with meningitis.

Preterm infants were those born before 37 weeks of gestation. The gestational age was determined by maternal dates or clinical assessment by Dubowitz score.

Maternal fever was defined as temperature of more than 37.8°C (in the absence of focal infection elsewhere and clinical dehydration). The clinical diagnosis of chorioamnionitis was made if 2 or the followings were present: maternal fever, fetal tachycardia, foul-smelling liquor and prolonged rupture of membrane.

Results

Vaginal GBS Carriage Rate Among Parturient Females

Over a 3-month period, one hundred and ninety-six parturient females who were admitted to the labour ward were randomly selected and screened. Nineteen isolates of GBS were obtained giving a vaginal carriage rate of 9.7% among parturient females (all races). Over this period, no neonate was affected by disease which could be attributable to GBS infection.

Early Neonatal GBS Septicaemia

Over an eleven-year period, 30 cases of early neonatal GBS septicaemia were treated: 28 cases were inborn and 2 outborn, giving an average of 2.7 cases per year. With 69 056 livebirths over the same period, the incidence of early neonatal GBS septicaemia worked out to be 0.41/1000 livebirths among inborn neonates.

The biodata of the mothers and neonates are summarised in Table I. Seventeen (57%) of the mothers were primigravida. Twenty-two (73%) of the neonates were delivered normally while 6 (20%) were delivered by Caesarean section for fetal distress. Table II shows the perinatal risk factors for early neonatal septicaemia. Prolonged rupture of membranes was noted in 5 (17%)

TABLE I: BIODATA OF MOTHERS, AND NEONATES WITH GBS SEPTICAEMIA (n = 30)

Inborn : outborn	28:2
Ethnic distribution	
Malay	14
Indian	
Chinese	
Eurasian	
Primigravida	17 (57%)
Gravida 2	6 (20%)
Gravida 4 or more	4 (13%)
Multiple pregnancies	0 (0%)
Deliveries	
Spontaneous vertex deliveries	22 (73%)
Caesarean section	6 (20%)
Forceps	1 (3%)
Induced, vaginal delivery	1 (3%)
Gestational age (mean $\pm$ SD)	37.5 $\pm$ 3.8 weeks
Birthweight (mean $\pm$ SD)	2540 $\pm$ 716 g
Low birthweight infants	14 (47%)
Preterm:term:post-term	12:17:1
Male:Female	16:14

TABLE II: PERINATAL RISK FACTORS FOR GBS SEPTICAEMIA (n = 30)

Prolonged rupture of membranes (>20 hours)	5 (17%)
Maternal pyrexia	3 (10%)
Chorioamnionitis	2 (7%)
Meconium-stained liquor	3 (10%)
Apgar scores	
≤ 5 at 1 min	6 (21%)
≤ 5 at 5 min	2 (7%)

* One neonate's Apgar scores were unknown.

of the cases, maternal pyrexia in 3 (10%) and clinical evidence of chorioamnionitis in 2 (7%). Peripartum ampicillin was prescribed to this group of mothers and that none of the mothers was infected by GBS postpartum.

Twelve (40%) of the neonates were preterm, while 14 (47%) were low birthweight. The male to female ratio was 1.1:1. Six (21%) of the neonates had Apgar scores of 5 or less at one minute after birth.

The onset of symptoms ranged from immediately after birth to four days of life with a mean of 8.3 $\pm$ 17.8 hours. Twenty-four (80%) presenting at or less than 6 hours of life. Significant signs were grunting, cyanosis and tachypnoea with or without apnoea (Table III). Nine (30%) neonates needed mechanical ventilation.

Positive surface swabs of at least moderate growth in two or more sites were found in 22/26 (85%) of all cases studied, while heavy growth in at least two sites was found in 11/26 (42%). Haematological abnormalities included anaemia (haemoglobin level of less than 15g%) in 13 (46%), thrombocytopenia in 9 (41%), and leukopenia

TABLE III: CLINICAL MANIFESTATIONS OF EARLY NEONATAL GBS SEPTICAEMIA (n = 30)

	n (%)
• Respiratory (grunting, cyanosis, tachypnoea or apnoea)	24 (80)
• Unstable temperature	3 (10)
Fever	6 (20)
Hypothermia	1 (3)
• Lethargy	5 (17)
• Pallor	2 (7)
• Jaundice	3 (10)
• Shock	2 (7)

or leukocytosis in 16 (57%) of neonates. Pneumonic changes were demonstrated in 19 (66%) neonates. All the GBS isolates were sensitive to penicillin, ampicillin, cephaloridine and gentamicin. Only one case had GBS isolated in the CSF. Two other neonates had marginally elevated polymorphs in their CSF which were otherwise normal biochemically and bacteriologically.

Overall, six (20%) neonates died. The mean age of onset of symptoms and signs was 4 hours (range 0 to 21 hours) and the mean duration of survival was 28.8 hours (range 12 to 38 hours). Five of these neonates were both preterm and low birthweight. Preterm and low birthweight infants had higher mortality than their term and heavier counterparts, 5/12 (42%) versus 1/18 (6%) ($P = 0.025$), and 5/14 (36%) versus 1/16 (6%) ($P = 0.06$), respectively although the latter was not statistically significant. In the deceased group more neonates required respiratory support soon after presentation 4/6 (67%) versus 6/24 (25%) of the group who survived.

Discussion

Although neonatal infection due to GBS was first recognised in 1958, GBS infection in human was considered rare, until the early seventies when McCracken² documented that GBS was a major cause of neonatal morbidity and mortality. Since then, the role of GBS in neonatal medicine remains important. The reasons for the emergence of GBS as a major pathogen among newborns are not well understood. It may be due to an increase in maternal colonisation, difference in the virulence of strains or simply that the disease had gained acceptance and became more widely recognised. In the past, it was possible that many GBS infections in infants might have been diagnosed as hyaline membrane disease.

In Malaysia, data on epidemiology and clinical aspects of neonatal septicaemia are scarce. Maternal genital tract colonisation by GBS has been reported to range from 2% to 30% in Western countries.³ It is well established that the carriage rate varies widely from country to country and even in the same place from time to time.^{3,4} A maternal genital GBS carriage rate of 9.7% is low when compared with data from Western countries.

This study was conducted over a 3-month period when a total of about 1800 pregnant mothers were admitted to the labour ward of University Hospital, Kuala Lumpur (an average of 600 deliveries per month takes place there). This represented 11% of the parturient mothers. This maternal carriage rate is comparable to that of Hong Kong's 7.4%.⁵

The incidence of neonatal GBS sepsis had been found to be as high as 5.4 per 1000 livebirths in the United States but data from the 1980s suggested that this might be decreasing to 2 per 1000 livebirths.³ In Europe, a lower incidence was observed, ranging from 0.7 to 1.5 per 1000 livebirths,⁴ while in Hong Kong, Chan et al⁵ reported an incidence of 0.58 per 1000 livebirths, similar to what was found in the present study (0.41 per 1000 livebirths). Obviously these two figures are lower than those reported from the United States and Europe. In our institution, postpartum mothers and their newborns are discharged early, within the first two to three days of life in most instances. There was a possibility that there were some mild cases who became ill soon after early discharge and were subsequently admitted to another hospital. The geographical variation in the prevalence of neonatal GBS sepsis could be due to bacterial factors and lower vaginal carriage rate of GBS in the different populations.³

Although the serotypes of GBS isolates were not determined in this study, Ngeow and Puthuchear,⁶ in their 1987 report on the distribution of GBS serotypes in Malaysia, noted that among the GBS isolates in neonates less than 10 days old, the predominant serotype was type III (61%), with 25% type Ic, 5.5% type Ib, 5.5% type II and 3% non-typeable strains. The absence of type Ia and the low occurrence of type II which together have been reputed to account for 30% of neonatal GBS septicaemia⁷ could explain the lower prevalence of neonatal GBS sepsis in the present series.

As maternal genital colonisation by GBS in our study was 9.7%, and assuming that 50% of infants of carrier mothers were colonised,³ then with 69 056 deliveries over an eleven-year period, the number of colonised neonates was expected to be 3349. With 28 neonates affected by GBS septicaemia, the attack rate of neonatal sepsis among colonised neonates was estimated to be 0.84 per cent. This attack rate is lower than those reported by other authors.^{8,9} Thus the risk of a Malaysian neonate colonised by GBS developing GBS septicaemia is lower than those reported by others.

Several risk factors have been identified previously for the pathogenesis of neonatal GBS sepsis in Caucasians, including low birthweight, prematurity, multiple pregnancies, prolonged rupture of membranes and maternal pyrexia.^{3,10,11} In the present study, 40% of infants were preterm and 47% had low birthweight. These figures were comparable to the experience of authors in

the United States and Europe, but contrary to what was found in Hong Kong, where prematurity and low birthweight infants accounted for 9% of infants with GBS septicaemia. The high proportion of primigravida mothers was expected as it is the policy of the hospital to accept high-risk pregnancies such as primigravida. Surprisingly, maternal pyrexia and prolonged rupture of membranes were not significant contributing factors in the development of GBS septicaemia in our experience, and none of the mothers had multiple pregnancies. Delivery by Caesarean section did not preclude neonates from GBS septicaemia, probably because of ascending infection.

Respiratory manifestation is the main feature observed in early onset GBS septicaemia. The onset of symptoms is typically early. Infected preterm infants usually present within 6 hours of life while term infants often do not manifest signs of the disease until after 24 hours of life.^{8,12} Tachypnoea, grunting and cyanosis with or without apnoea are the usual presenting symptoms and signs. Although infiltrates suggestive of congenital pneumonia are often described on chest radiographs, radiological appearances indistinguishable from that of hyaline membrane disease are seen in more than half of the cases. Thus, chest radiographs are of limited value in differentiating GBS pneumonia from other forms of pneumonia.^{13,14}

Meningitis is seen in about a third of cases of early onset GBS septicaemia but is most commonly associated with late-onset disease. The presentation is similar to that of neonatal meningitis with non-specific symptoms and signs. Neurological sequelae are, however, seen in about a third of survivors of early onset disease, ranging from hearing loss to cortical blindness.¹⁵ In this study, meningitis was uncommonly seen as only 1 (3%) had GBS isolated in the CSF, while 2 had raised polymorph count in the CSF. Lumbar puncture was not performed routinely as part of a septic work-up. It was indicated in infants with symptoms and signs of irritability, seizure and lethargy. However, these infants were usually too unstable to withstand lumbar puncture and they rapidly succumbed to the illness. Thus, meningitis in this category of neonates might not have been diagnosed. In order to improve the diagnostic rate for GBS meningitis, lumbar punctures were performed in neonates whose blood cultures were positive. However, in this group of neonates, no evidence of meningitis was found.

Leukocytosis, relative leukopenia, absolute neutropenia and an increase in immature neutrophils are common in early neonatal septicaemia but are non-specific. The ratio of absolute immature neutrophils to absolute total neutrophils was found to be elevated in 90% of infected neonates.¹⁶ Our results also revealed that a positive surface swab with heavy and moderate growth in at least two sites was associated with early GBS

septicaemia, as 80% of all cases studied had at least moderate growth in 2 sites and 40% of them had heavy growth in at least 2 sites.

Treatment must be initiated immediately when a diagnosis of GBS septicaemia is suspected, after appropriate samples have been taken, as this condition often runs a rapid fulminating course, and early treatment improves the prognosis.^{3,17} Since all the GBS isolates in our experience were sensitive to penicillin and ampicillin, one of them should be included in the antibiotic regimen. An amnioglycoside should be added because of the possibility of penicillin tolerance, for the coverage of possible gram-positive organism and a possible synergistic effect with penicillin during the initial phase of therapy.

Early neonatal GBS septicaemia causes a high mortality rate ranging from 20% to 50%,¹⁸ but improved case fatality rates of 9.1%⁴ and 15%¹⁹ were reported in recent years. In the present study, there were 6 mortalities (20%), five of whom were both preterm and low birthweight infants. Overall, preterm and low birthweight infants were found to have higher mortality than their term and heavier counterparts.^{19,20}

Prophylactic measures have been proposed, including penicillin chemoprophylaxis and immunotherapy.^{3,18} However, the incidence and attack rates of neonatal GBS septicaemia were low in our study. Six mortalities over eleven years meant one death in two years was due to GBS septicaemia. Thus, mass screening and chemoprophylaxis are not cost-effective and not warranted. Efforts should be directed to those with perinatal risk factors for neonatal septicaemia in general and early treatment of symptomatic cases. Neonates, especially preterm and low birthweight, who develop respiratory distress soon after birth should be treated for early neonatal GBS septicaemia.

In conclusion, an experience of GBS septicaemia over an eleven-year period involving 30 cases was described. Respiratory manifestation was the main presentation. All the GBS isolated were sensitive to penicillin and ampicillin. As the vaginal GBS carriage rate, the prevalence of neonatal GBS septicaemia and the case-fatality rate were low, mass screening for vaginal GBS carriage, and chemoprophylaxis in neonates were not justified. The initial management of suspected early GBS septicaemia should be in line with suspected septicaemia in general, as no definite perinatal risk factors for early neonatal GBS septicaemia were identified.

REFERENCES

1. Nyhan W L, Fousek M D. Septicaemia of the newborns. *Pediatrics* 1958; 22:268-78.
2. McCracken G. GBS: New challenge in neonatal infection. *J Pediatrics* 1973; 82:703-6.

3. Baker C J, Edwards M S. Group B streptococcal infections. In: Remington J S, Klein J O, editors. *Infections Diseases of the Fetus and Newborn Infant*. 3rd ed. Philadelphia: WB Saunders, 1990:742-811.
4. Mayon-White R T. The incidence of GBS disease in neonates in different countries. In: Christensen K K, Christensen I', Ferrieri I', editors. *Antibiotics and Chemotherapy: Neonatal Group B Streptococcal Infection*. Basel: Karger, 1985: 17-27.
5. Chan S H, Lan S P, Fok T F, Liang S T. Early onset neonatal Group B streptococcal infection in Hong Kong. *Asia Oceania J Obstet Gynaecol* 1986; 12:341-6.
6. Ngeow Y F, Puthuchear S D. Distribution of group B streptococcal serotypes in Malaysia. *J Trop Med Hyg* 1987; 90:193-6.
7. Baker C J, Barrett F F. Group B streptococcal infections in infants: The importance of the various serotypes. *JAMA* 1974; 230:1158-60.
8. Anthony B F, Okada D M. The emergence of group B streptococci in infection of the newborn infant. *Annu Rev Med* 1977; 28:355-69.
9. Baker C J. Summary of the workshop on perinatal infections due to group B streptococcus. *J Infect Dis* 1977; 136:137-52.
10. Pass M A, Khare S, Dillon H C Jr. Twin pregnancies: incidence of group B streptococcal colonisation and disease. *J Pediatr* 1980; 97:635-7.
11. Boyer K M, Gadzala C A, Burd L, Fisher D E, Paton J B, Gotoff S B. Selective intrapartum chemoprophylaxis of neonatal group B streptococcal early-onset disease. I. Epidemiologic rationale. *J Infect Dis* 1983; 148:795-801.
12. Baker C J. Group B streptococci infections. *Adv Intern Med* 1980; 25:475-501.
13. Lilien L D, Harris V J, Pildes R S. Significance of radiographic findings in early-onset group B streptococcal infection. *Pediatrics* 1977; 60:360-3.
14. Vollman J H, Smith W L, Ballard E T, Light I J. Early onset group B streptococcal disease: clinical, roentgenographic and pathologic features. *J Pediatr* 1986; 89:199-203.
15. Haslam R H A, Allen J R, Dorsen M M, Kanofsky B L, Mellits D, Norris D A. The sequelae of group B β -hemolytic streptococcal meningitis in early infancy. *Am J Dis Child* 1977; 131:845-9.
16. Manroe B L, Rosenfeld C R, Weinbey A G, Browae R. The differential leukocyte count in the assessment and outcome of early-onset neonatal group B streptococcal disease. *J Pediatr* 1977; 91:632-7.
17. Anonymous. Neonatal infection with group B streptococci [editorial]. *Lancet* 1981; 2:181-2.
18. Dashefsky B, Wald E R, Green M. Prevention of early onset group B streptococcal sepsis. *J Pediatr* 1988; 112:1039-42.
19. Sjoberg I, Hakansson S, Eriksson A, Schollin J, Stjerastedt B, Tessin I. Incidence of early onset group B streptococcal septicaemia in Sweden 1973 to 1985. *Eur J Clin Microbiol Infect Dis* 1990; 9:276-8.
20. Payne N R, Burke B A, Day D L, Christensen P D, Thompson T R, Ferrieri P. Correlation of clinical and pathologic findings in early onset neonatal group B streptococcal infection with disease severity and prediction of outcome. *Pediatr Infect Dis J* 1988; 7:836-47.