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Long-Term Outcomes Following Infant Group B Streptococcal Sepsis and Meningitis in Hong Kong

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Abstract

Our single hospital report on 8 infants with development delays from 71 neonatal Group B Streptococci (GBS) meningitis/sepsis cases during 2007-2017 in Hong Kong draws attention to the limited information on long-term sequelae after early-life GBS infection in Asia. Two meningitis survivors showed more extreme condition, such as epilepsy. Strategies to reduce such burden in infants remains to be sought.

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Introduction

Approximately 219,000 invasive *Streptococcus agalactiae* (GBS) infections occur in infants worldwide, causing over 90,000 deaths and 57,000 stillbirths [1]. GBS disease poses a substantial burden among infants causing early-onset (EOD) and Late-Onset Disease (LOD) with high mortality [2,3]. Infants that survived GBS infection continue to have risks of morbidity and mortality through their first five years of life [4]. Moreover, 40% of these survivors from meningitis were prone to develop neurological conditions including cerebral palsy and epilepsy [5]. Thus understanding the long-term sequelae of early-life GBS meningitis/sepsis is essential to help predict those at risk, especially in Asia where this is scarcely reported. This study reviewed cases of invasive GBS disease among infants and their long-term outcomes.

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All cases of infants (0-12 months of age) hospitalised at the Prince of Wales Hospital, Hong Kong, with a positive GBS culture from blood or body fluids during the 11-year period (2007-2017) were reviewed. Clinical records were extracted through the Clinical Data Analysis and Reporting System (CDARS). Long-term outcome data related to GBS sepsis/meningitis and infection were extracted (including re-admission, follow-up visits, and any developmental delays). Infants with GBS disease within 6 days of life were considered EOD, while those who were infected between 7th and 89th days of life were LOD. Univariate analysis was conducted by Chi-square or Fisher's exact test using the Statistical Package for Social Sciences, SPSS (IBM, v25). A *P*-value of <0.05 was considered statistically significant. The study was approved by the Joint Chinese University of Hong Kong – New Territories East Cluster Clinical Research Ethics Committee (CREC NO.:2018.509).

A total of 71 infants admitted for GBS sepsis/meningitis between 2007 and 2017 were reviewed. The highest number of admissions occurred in 2011 (n=15) and the lowest in 2015 (n=1), with a mean of 6.45 admissions per year. A majority of the admissions were for GBS sepsis (n=51, 71.8%) (Table 1). There were 20 (28.2 %) admissions for meningitis. The percentages of EOD and LOD cases were 46.5% (n=33) and 53.5% (n=38) respectively. Discharge details were reviewed for 69 cases (two records were not available). Mortality occurred in 5 cases (7.25%), with 3 and 2 from meningitis and sepsis respectively. Sixty-one cases had follow-up data available post-discharge with no re-admission among EOD infants, but 22.9% (n=8) of the LOD infants were re-admitted for further antimicrobial treatment. Only six (9.84%) cases had been referred to the Child Assessment Centre (CAC) for specialised assessment on paediatric rehabilitation and developmental growth. Based on hospital re-admissions and follow-up, developmental delay occurred in 8 cases (13.1%), half of whom had previously suffered from GBS meningitis (20.0% among meningitis cases) and the other half from sepsis (9.76% among sepsis cases). Developmental delay was observed in EOD and LOD (19.2%, n=5 and 8.57%, n=3 respectively). Among those 8 cases (Table 2), 4 developed autism spectrum disorder (ASD) (Patients 484U, 780P, 256O and 180T), of which 3 survived from GBS sepsis. Two children detected signs of hearing impairment, of which one developed auditory neuropathy post-GBS meningitis (Patient 793S), and the other failed an initial hearing test post-early-life GBS sepsis, but no follow-up data were available (Patient 405U). The remaining 2 cases had more extreme developmental delay following GBS meningitis as brain imaging displayed areas of post-infection atrophic changes. One case showed difficulty in speech and learning, attention-deficit/hyperactivity disorder (ADHD) and epilepsy (Patient 229T). The other case showed signs of gross developmental delay and developed cerebral palsy, intellectual disability, and intractable epilepsy (Patient 314M).

Universal screening programme for GBS in pregnant women was launched in January 2012 as part of antenatal services in Hong Kong public health [6], but this would not reduce the burden for LOD. A recent meta-analysis, which mostly included studies from the United States, estimated 32% of early-life GBS meningitis survivors had developmental impairment [7]. This is slightly higher than our rates (20%), but it also reflects geographical differences and paucity of data elsewhere. Hospital follow-up may only detect medical complications or gross developmental changes, while minor development deviation may be neglected. Thus, all our meningitis cases would benefit with referral to the CAC for specialised assessment. The small cohort of our single centre study failed to reach statistical significance for most of our comparative analyses. Follow-up data of 10 cases were missing, which may also contribute to an underestimation of long-term sequelae. Infants admitted from 2015 onwards are still relatively young with shorter follow-up period, thus may not be representative. A multi-centre study to follow up all infants with GBS disease in longer term can more comprehensively assess the long-term sequelae amongst GBS infected infants.

Conclusion

In conclusion, invasive GBS disease remains a significant burden amongst Hong Kong infants. Strategies to reduce LOD incidences is required. Both GBS meningitis and sepsis contribute to developmental delay. Referral to CACs with early detection and support for growth developmental delay is warranted.

Table 1: Patient characteristics, disease and outcomes.

	Total N (%)	EOD N (%)	LOD N (%)	*P-value* (EOD vs LOD)
No. of cases (71)	71 (100)	33 (46.5)	38 (53.5)	-
Sepsis (Bacteremia)	51 (71.8)	26 (51.0)	25 (49.0)	0.23
Meningitis	20 (28.2)	7 (35.0)	13 (65.0)	0.23
Mortality at discharge[a]	5 (7.25)	4 (12.9)[b]	1 (2.63)	0.17
Sepsis group (bacteremia)[a]	2 (4.08)[b]	1 (4.17)[b]	1 (4.00)	1.00
Meningitis group	3 (15.0)	3 (42.9)	0 (0.00)	**0.031**
No. cases with any post discharge follow-up	61 (88.4)	26 (42.6)	35 (57.4)	-
Sepsis (bacteremia) group	41 (80.4)	19 (46.3)	22 (53.7)	-
Meningitis group	20 (100)	7 (35.0)	13 (65.0)	-
GBS related re-admissions	8 (13.1)	0 (0.00)	8 (22.9)	**0.009**
Sepsis group (bacteremia) (n=41)	5 (12.2)	0 (0.00)	5 (22.7)	0.051
Meningitis group (n=20)	3 (15.0)	0 (0.00)	3 (23.1)	0.521
No. referred to Child Assessment Center	6 (9.84)	2 (7.69)	4 (11.4)	1.00

No. cases with developmental delay	8 (13.1)	5 (19.2)	3 (8.57)	0.22
Sepsis group (bacteremia) (n=41)	4 (9.76)	3 (15.8)	1 (4.55)	0.321
Meningitis group (n=20)	4 (20.0)	2 (28.6)	2 (15.4)	0.587

[a] Only 69 cases included, 2 with missing discharge details

[b] 2 cases from total with missing discharge details

P values in bold indicate statistical significance (*P* <0.05)

Table 2: Characteristics of patients with developmental delay post early-life invasive GBS disease.

Patient code	GBS related disease during first admission	Year of admission	Admission age (days)	Early/ late onset	MRI/CT scan (outcome)	Age during first detection of developmental delay (months)	Subsequent epilepsy/ seizure	Record of latest follow up (Year)	Age at latest follow up (Years)	Developmental delay/ disability
314M	Meningitis	2007	0	Early	Yes (Cerebral abnormalities detected)	4	Yes	2019	11	Cerebral palsy, intellectual disability, intractable epilepsy
229T	Meningitis	2009	43	Late	Yes (Cerebral abnormalities detected)	7	Yes	2019	10	Speech and learning slow, ADHD[a], epilepsy
484U	Sepsis (Bacteremia)	2009	1	Early	No	49	No	2019	9	ASD[b] and ADHD[a]
780P	Meningitis	2009	20	Late	Yes (uneventful)	31	No	2017	7	ASD[b], speech delay
265O	Sepsis (Bacteremia)	2009	1	Early	No	66	No	2019	9	ASD[b]
405U	Sepsis (Bacteremia)	2011	0	Early	No	2	No	2019	7	Failed a hearing test- no follow up data available
793S	Meningitis	2012	0	Early	No	5	No	2018	6	Auditory neuropathy
180T	Sepsis (Bacteremia)	2014	32	Late	No	Unknown	No	2018	4	Childhood autism

[a]**ADHD:** Attention-deficit/hyperactivity disorder; [b]ASD: Autism spectrum disorder

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