TREND AND CUT-OFF POINT OF NEONATAL MENINGITIS ONSET IN A HIGHLY MULTIDRUG-RESISTANT AREA

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Abstract. In order to compare the trend in meningitis between 1991-2002 (period 1) and 2003-2014 (period 2) and to identify a cut-off point in culture-proven meningitis, we performed a retrospective comparative study in a neonatal intensive care unit (NICU) in Thailand. Over a total of 24 years, the number of patients, episodes and pathogenic organisms of culture-proven meningitis was 46, 54, and 62, respectively. Prevalence of culture-proven meningitis cases was 0.037% of live births and 0.52% of NICU-admitted neonates. Median (interquartile range) gestational age (GA) and birthweight (BW) was 35 (7) weeks and 2,045 (1,208) g, respectively. The case fatality rate was 21.7% (10/46). In period 2, preterm (odds ratio (OR) = 6.4) and low BW (OR = 7.8) are significantly higher than in period 1 (p = 0.007 and 0.006, respectively). *Acinetobacter baumannii* was the most common (16%) causative organism and cause (40%) of death, which increased significantly in period 2 (p = 0.03). Within 48 hours of birth, no multidrug resistant (MDR) organisms were found (0/2); however, within 72 hours MDR organisms were found in 44% (7/16) of the subjects. In conclusion, prematurity was a risk factor of meningitis in more recent period. Early onset meningitis should have a cut-off within 48 hours in areas with high frequency of high MDR organisms.

Keywords: *Acinetobacter baumannii*, meningitis, multiple drug resistance, neonate, sepsis

INTRODUCTION

Meningitis is a life threatening disease especially in neonates that leads to high mortality and morbidity. Long-term sequelae of meningitis are troublesome, with moderate to severe disability rates of 19.8-25.5% in patients who survived (Bedford *et al*, 2001; Stevens *et al*, 2003). Factors involved in an organism's cause of meningitis include colonization from the mother or environment, genetics of immune response and laboratory techniques. In various situations, certain pathogenic organisms have been the major players contributing to the syndrome (Thatrimontrichai *et al*, 2014).

Multidrug-resistant (MDR) organisms have rapidly emerged as a serious threat to critically ill neonates (Thatrimontrichai *et al*, 2013; *ibid*, 2016). A cut-off point between early and late onset neonatal

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sepsis (bacteremia and meningitis) is not well defined, *eg* 2, 3, or 7 days (Shane *et al*, 2017). The combined use of ampicillin and gentamicin as empirical antimicrobials for early onset sepsis is recommended (Shane *et al*, 2017); however, this regimen may not be suitable in treating MDR bacteria.

In places with a prevalence of MDR microbial pathogens other antimicrobial options should be considered based on local epidemiology for treatment of early and late onset infection. Early intervention with appropriate intensive care support is the most beneficial in reducing mortality and morbidity as well as in improving neurodevelopmental outcome. This study identified the trend and cut-off point in culture-proven meningitis in a Thai neonatal intensive care unit (NICU).

MATERIALS AND METHODS

Study site and subjects

This study was conducted at the NICU, Songklanagarind Hospital, Songkhla, Thailand. The NICU is a level III, single 15-bed room in a university-affiliated teaching hospital at Prince of Songkla University which is a referral center for 14 provinces of southern Thailand.

Subjects were identified from source records of Songklanagarind Hospital clinical microbiological laboratory. All records were reviewed to ensure that all eligible subjects were identified. The medical records of all neonates with meningitis obtained at any time during admission to the NICU from January 1, 1991 to December 31, 2014 were included in the study. The obstetric and neonatal recorded data of the patients were: demographic features, clinical manifestations, antimicrobials used, cerebrospinal fluid (CSF) findings, antimicrobial susceptibilities, and outcomes. In order to compare changes over time, the incidence and case fatality rate of meningitis in neonates were divided into two equal periods, namely 1991-2002 (period 1) and 2003-2014 (period 2). A cut-off point in culture-proven meningitis within 48 or 72 hours after birth to consider empirical antimicrobial use in neonatal meningitis was the principle objective of the study.

The study was approved by the Ethics Committee Board of the Faculty of Medicine, Prince of Songkla University (REC. 58-263-01-1).

Study design

Preterm and very preterm is defined as gestational age (GA) of 33-36 and 24-32 weeks, respectively, while low birthweight (LBW) and very low birthweight (VLBW) were defined as 1,500-2,499 and 1,000-1,499 g, respectively. Early onset meningitis (EOM) and late onset meningitis (LOM) were based on CSF cultures obtained from lumbar punctures at 48 (EOM_{48} and LOM_{48}) and 72 (EOM_{72} and LOM_{72}) hours after birth, respectively. Criteria for diagnosis of ventilator-associated pneumonia (VAP) followed the Centers for Disease Control and Prevention (CDC) and the National Healthcare Safety Network (NHSN) guidelines for infants <1 year old (CDC and NHSN, 2018). Clinical presentations at onset of meningitis were categorized as asymptomatic but with high risk of infection, *eg* maternal fever or chorioamnionitis, and symptomatic of meningitis, VAP or bacteremia. Previous neurological surgery is defined if the patient has a ventriculoperitoneal shunt or myelomeningocele/encephalocele repair.

Meningitis is defined as a positive CSF culture with either gram-negative or gram-positive (except commensal) organ-

isms. The commensal organisms are *Aerococcus* spp, *Bacillus* spp, coagulase-negative Staphylococci (CoNS), *Corynebacterium* spp, group A Streptococci (GAS)/viridans Streptococci, *Micrococcus* spp, *Propionibacterium* spp, and *Staphylococcus epidermidis*. Commensal organisms are the true pathogens if there is at least one of the following criteria: seizure (before or after 7 days of positive CSF culture), bacteremia (same organism and antibiogram before or after 7 days of positive CSF culture), repeated CSF culture (same organism and antibiogram within 7 days of positive CSF culture), CSF white blood cell count >19/mm^3 plus CSF red blood cell count <1,000/mm^3, intraventricular hemorrhage, ventriculoperitoneal shunt (before positive CSF culture), history of central nervous system (CNS) surgery (before positive CSF culture), CNS anomaly (before positive CSF culture), or died within 7 days of positive CSF culture. Contamination is defined if the cultured commensal organism(s) is(are) not included in the above list.

Bacteria (*Acinetobacter* spp, Enterobacteriaceae, *Enterococcus* spp, *Pseudomonas aeruginosa*, and *Staphylococcus aureus*) were considered MDR when the isolate was not susceptible to at least one agent among at least three antimicrobial categories, namely, aminoglycosides, carbapenems, cephamycins, extended-spectrum cephalosporins, fluoroquinolones, folate pathway inhibitors, glycylcyclines, monobactams, non-extended spectrum cephalosporins, penicillins, penicillins/beta-lactamase inhibitors, phenicols, phosphonic acids, polymyxins or tetracyclines (Magiorakos *et al*, 2012). In clinical practice, combination antimicrobials (combinations of penicillin or ampicillin or cefotaxime and gentamicin) are used for early onset meningitis.

The data were categorized by the numbers of patients with meningitis, episodes of meningitis (additional pathogens recovered 14 days later were added to the same episode) and pathogenic organisms. GA, birthweight (BW), sex, location of birth, mode of delivery, Apgar scores, case fatality rate, and length of hospital stay of patients with meningitis were recorded. Other variables were recorded as episodes of meningitis. Percent susceptibilities of pathogenic organisms were also noted.

Statistical analysis

We estimated 84 neonates, 42 in each time period, would need to be enrolled in the study to have 80% power of detecting a difference of at least 15% in the rate of MDR meningitis, assuming a rate of 15% in period 1 and 30% in period 2, with a 0.05 significance level. The R program (version 2.14.1; Free Software Foundation, Boston, MA) was used to develop a database of categorical and continuous variables. Categorical variables are presented as frequency and percentage and compared using χ^2 test or Fisher's exact test. Continuous variables are presented as mean (± SD) and median (interquartile range; IQR) and compared using Mann–Whitney *U* test or Student's *t*-test. All *p*-values are 2 tailed and a *p*-value <0.05 is considered statistically significant, and 95% confidence intervals (CIs) are computed for independently significant variables over the two time periods.

RESULTS

One hundred organisms were found in CSF cultures over the 24-year period. Thirty-eight organisms were excluded due to contamination. During the 24-year study period, the number of patients, episodes, and pathogenic organisms of culture-proven meningitis was 46, 54,

Table 1
Comparison of characteristics and outcomes between period 1 (1991-2002) and 2 (2003-2014) in neonatal meningitis at a neonatal intensive care unit, Songklanagarind Hospital, Songkhla.

Characteristic	Period 1 No. of infants (%) (n = 27)	Period 2 No. of infants (%) (n = 19)	p-value
Gestational age (week)[a]	37 (8)	32 (7)	0.02
Preterm	11 (41)	16 (84)	0.006
Very preterm	3 (11)	8 (42)	0.03
Birth weight (g)[a]	2,050 (1,420)	1,540 (1,093)	0.006
Low birth weight	10 (37)	15 (79)	0.007
Very low birth weight	4 (15)	8 (42)	0.049
Male	9 (33)	10 (53)	0.23
Inborn	14 (52)	11 (58)	0.77
Cesarean section	10 (37)	9 (47)	0.55
Multiple gestations	4 (15)	5 (26)	0.46
Death	4 (15)	6 (32)	0.28
Length of hospital stay (day)[a]	33 (52)	18 (56)	0.73
Length of surviving hospital stay (day)[a]	37 (54)	45 (57)	1.00
Characteristic	Period 1 No. of infants (%) (n = 35)	Period 2 No. of infants (%) (n = 19)	p-value
Actual weight at onset of meningitis (g)[a]	2,700 (1,260)	1,840 (1,130)	0.001
Age at onset of meningitis (dd:hh)[a]	6:19 (13:10)	7:22 (15:01)	1.00
Early-onset meningitis (before 72 hours after birth)	7 (20)	3 (16)	1.00
Early-onset meningitis (before 7 days)	17 (49)	6 (32)	0.26
Clinical presentation			
Meningitis	13 (37)	14 (74)	0.02
Asymptomatic (high risk)	12 (34)	2 (10)	0.10
Bacteremia	10 (29)	1 (5)	0.07
Ventilator associated pneumonia	0 (0)	8 (42)	<0.001
Previous neurological surgery	15 (43)	2 (10)	0.02
Bacteremia (same organisms)	7 (20)	9 (47)	0.06
Multidrug-resistant organisms	8/25 (32)	7/12 (58)	0.16

[a]Median (interquartile range).

and 62, respectively. Twenty-five (54%) neonatal meningitis cases were inborn patients. A total of 68,053 infants were born at Songklanagarind Hospital and 8,866 (13.03%) were admitted to the NICU. The overall cumulative prevalence of culture-proven meningitis for inborn neonates was 0.37 cases per 1,000 live births and 0.52% for NICU-admitted neonates. The prevalence of MDR meningitis was 41% (15/37 episodes). Median (IQR) BW, GA, and Apgar score at one and five minutes of life was 2,045 (1,208) g, 35 (7) weeks, 8 (3), and 9 (2), respectively. Case fatality

rate was 21.7% [10/46; 4 cases with *Acinetobacter baumannii* infection, 2 with *Klebsiella pneumoniae*, and 1 each with *Bacillus* sp, *Pseudomonas pseudoalcaligenes*, *Sphingobacterium* sp, and *Streptococcus* (not group B or D)].

Neonatal meningitis in period 2 shows significantly lower GA, BW, and actual weight at onset of meningitis than in period 1 (Table 1). Preterm [odds ratio (OR) = 7.8; 95% CI: 1.8-33.3, $p = 0.006$], very preterm (OR = 5.8; 95% CI: 1.3-26.3, $p = 0.03$), LBW (OR = 6.4; 95% CI: 1.7-24.4, $p = 0.007$), VLBW (OR = 4.2; 95% CI: 1.03-16.9, $p = 0.049$), clinical presentation with meningitis (OR = 4.7; 95% CI: 1.4-16.2, $p = 0.02$), and VAP (OR = 4.1; 95% CI: 2.5-7.0, $p < 0.001$) of neonatal meningitis in period 2 were significantly higher than in period 1. However, previous neurological surgery (OR = 0.2; 95% CI: 0.03-0.8, $p = 0.02$) in period 2 was significantly lower than in period 1. There was no difference in case fatality rate between the two time periods. The median (IQR) time to positivity (d:hh) was 3:15 (3:00). Thirty percent (16/54; 6 with *A. baumannii* infection, 2 each with *K. pneumoniae*, *Staphylococcus aureus* and *Staphylococcus epidermidis*, and 1 each with *Bacillus* sp, *P. pseudoalcaligenes*, *Serratia marcescens*, and *Sphingobacterium* sp) of neonatal meningitis had bacteremia. Fifteen percent [8/54; 5 with *A. baumannii* infection, and 1 each with *K. pneumoniae*, *Streptococcus* (not group B or D) and *S. aureus*] of neonatal meningitis had VAP.

Among the 62 pathogenic organisms cultured, 23 (37%) were gram-positive (GPB) (*Enterococcus* being most common) and 39 (63%) gram-negative (GNB) (*A. baumannii* most common) (Table 2). Among EOM_{48} (1 each of *Bacillus* sp, *Enterococcus* sp, GBS, *K. pneumoniae* and *P. pseudoalcaligenes*) and EOM_{72} (5 *K. pneumoniae*, 4 *A. baumannii*, 3 *Escherichia coli*, 2 *Enterococcus* spp, and 1 each of *Bacillus* sp, GBS, *Proteus mirabilis*, *P. pseudoalcaligenes*, and *Salmonella* sp) 40% and 47% were resistant to combination antimicrobials, respectively. Zero percent and 44% MDR among EOM_{48} and EOM_{72}, respectively, were resistant to combination antimicrobials. The top three pathogenic organisms among LOM_{48} and LOM_{72} were *A. baumannii*, *E. coli*, and *Enterococcus* spp. Prevalence of *A. baumannii* meningitis during period 1 (7/22, 32%) was significantly higher than period 2 (3/40, 7%) (OR = 5.8; 95% CI: 1.3-25.3, $p = 0.03$); however, there were no significant differences in the other organisms.

An antibiogram showed that *A. baumannii*, *Enterococcus* sp, *P. pseudoalcaligenes*, and *Sphingobacterium* sp were susceptible to colistin, vancomycin, ofloxacin, and ciprofloxacin, respectively. Of 44 pathogenic organisms tested against carbapenems, 10/44 (23%) (5 *A. baumannii*, 3 *Enterococcus* spp and 1 each of *P. pseudoalcaligenes* and *Sphingobacterium* sp) were resistant to imipenem and/or meropenem. *A. baumannii* was the most common (16% and 40%) causative organism and cause of death, respectively, with 56% (5/9) resistant to carbapenem (CRAB), which were found in 60% (3/5) of fatal neonatal meningitis. Three neonates with CRAB meningitis were treated with colistin as empirical antimicrobial, and subsequent lumbar punctures revealed microbiologically cure 72 hours after the positive culture.

DISCUSSION

The overall prevalence of culture-proven meningitis (0.37/1,000 live births) and case fatality rate (21.7%) over the

Table 2
Pathogenic organisms causing neonatal meningitis at a neonatal intensive care unit, Songklanagarind Hospital, Songkhla during 1991-2014.

Organism	Number	MDR	Antimicrobial susceptibility									
			Ampicillin	Vancomycin	Cefotaxime	Ceftazidime	Sulperazone	Gentamicin	Amikacin	Imipenem	Meropenem	Colistin
Gram-positive	23	3/11	6/10	17/17				1/7		3/6		
Enterococcus species	7	3/7	3/6	6/6				0/6		3/6		
Staphylococcus aureus	4	0/4		2/2								
Streptococcus (not group B or D)	3		2/3	3/3								
Staphylococcus epidermidis	3			3/3								
CoNS	3			3/3								
Bacillus species	2							1/1				
GBS	1		1/1									
Gram-negative	39	11/32			14/30	23/39	2/5	11/17	11/17	28/35	2/7	5/5
Acinetobacter baumannii	10	5/10			0/6	3/10	0/3	1/4	1/4	4/9	0/5	5/5
Escherichia coli	8	2/8			4/6	6/8	1/1	3/3	3/3	8/8	1/1	
Klebsiella pneumoniae	6	3/6			2/6	1/6		1/3	2/3	5/5		
Pseudomonas aeruginosa	3	0/3				3/3		3/3	3/3	3/3		
Moraexella species	3				2/3	3/3		1/1	1/1	3/3		
Proteus mirabilis	2	0/2			2/2	2/2		2/2	1/1			
Sphingobacterium species	2				0/2	1/2				1/2		
Enterobacter cloacae	1	1/1			1/1	1/1				1/1		
Flavobacterium species	1				1/1	1/1	1/1			1/1	1/1	
Pseudomonas pseudoalcaligenes	1				0/1	0/1		0/1	0/1	0/1		
Salmonella species	1	0/1			1/1	1/1				1/1		
Serratia marcescens	1	0/1			1/1	1/1			0/1	1/1		
Total	62	13/43	6/10	17/17	14/30	23/39	2/5	12/24	11/17	31/41	2/7	5/5

CoNS, coagulase-negative *Staphylococcus*; GBS, group B *Streptococcus*; MDR, multidrug resistance.

24-year study period were higher than previous studies in developed countries. For instance, the prevalence of meningitis in a regional UK study was 0.21-0.25 cases per 1,000 live births and case fatality rate decreased from 29% to 10% over a period of 10 years (Hristeva *et al*, 1993; Holt *et al*, 2001; Galiza and Heath, 2009). In other developed countries case fatality rate of meningitis was 10-13% (Holt *et al*, 2001; Chang *et al*, 2003; Galiza and Heath, 2009; Gaschignard *et al*, 2011; Kavuncuoglu *et al*, 2013), while it was higher (40-58%) in developing countries (Furyk *et al*, 2011).

As a neonatal care unit becomes more sophisticated the survival rate of preterm infants rises as a preterm infant is considered an immune-compromised host who requires many antimicrobials treatment and a longer hospital stay. Thus, lower GA, BW, actual weight, and VAP were significantly higher in period 2 compared to period 1. However, our hypothesis of meningitis with previous neurological surgery is that it is due to a higher coverage of folic acid supplement during pregnancy, more terminations of pregnancy if there was an abnormal CNS finding from prenatal diagnosis and a lower incidence of severe intraventricular hemorrhage from improved preterm care.

The most common pathogen is group B *Streptococcus* (GBS) and *Streptococcus agalactiae* for EOM and GNB for LOM (Heath *et al*, 2003; Furyk *et al*, 2011; Gaschignard *et al*, 2011). However, studies in Asia showed that the most common causative organisms were *E. coli* in EOM and GBS in LOM (Chang *et al*, 2003; Chang *et al*, 2014;). Studies in Thailand reported *P. aeruginosa* (Chotpitayasunondh, 1994) and *E. coli* (Searejitima, 2007; Pattarathitikul, 2012) as the most common etiology of meningitis in the neonatal period. GBS neonatal meningitis is rare in Thailand with reports of 2-9 cases (Chotpitayasunondh, 1994; Yossuck and Preedisripipat, 2002; Thatrimontrichai *et al*, 2017a). *Listeria* meningitis in neonates has never been reported in Thailand (including the current study). In our study, the most common pathogens in EOM and LOM were *K. pneumoniae* and *A. baumannii*, respectively, while in meningitis *Enterococcus* and *A. baumannii* were the most common GPB and GNB, respectively. Only one patient was infected with GBS. *A. baumannii* had a significantly higher trend in period 2 but incidences of MDR organisms were not significantly different between the two survey periods.

This study demonstrates that very preterm and VLBW infants with meningitis increased significantly and *A. baumannii* meningitis had the highest incidence and was increasingly prevalent among NICU patients in Thailand, replacing *P. aeruginosa* detected in the 1980s (Chotpitayasunondh, 1994). The incidence and mortality of CRAB meningitis increased similarly as with CRAB bacteremia and VAP in neonates (Thatrimontrichai *et al*, 2013; *ibid*, 2016; *ibid*, 2017b). Colistin was considered if CRAB or a pan drug-resistant organism caused meningitis; however, colistin use was off-label for the neonatal period (Saleem *et al*, 2011; Thatrimontrichai *et al*, 2014). Although colistin penetration in CSF appears to increase significantly in pediatric meningitis, the concentrations may be inadequate for treatment of bacterial infections (Antachopoulos *et al*, 2010). Intraventricular colistin administration due to *A. baumannii* CNS infection is more effective than intravenous therapy alone, but more information is needed to determine long term safety and efficacy of colistin in neonates (De Bonis *et al*, 2016).

We recommend changing the cut-off point in "early *vs* late onset of meningitis

or sepsis in neonate" from "72 hours or 3 days" to "48 hours" after birth when empirical antimicrobial use is under consideration. MDR organisms were found in 44% of EOM if the cut-off was 72 hours and may not be covered by combination antimicrobials. The choice of empirical antimicrobial should cover MDR organisms as well as organisms that have a high incidence of drug resistance in the region. Hence, empirical antimicrobial use was "ampicillin and gentamicin" in EOM_{48} and "cefotaxime and amikacin" or "meropenem" in LOM_{48}.

However, this study suffers from a number of limitations. First, it was a retrospective survey with a small sample size. Second, there was no standard definition for endogenous infection and an incomplete CSF profile with only positive CSF cultures (culture-proven meningitis) and no inclusion of negative CSF cultures with CSF pleocytosis as there was no criterion to diagnose "CSF pleocytosis" in term and preterm neonates due to inconclusive numbers of white blood cells in the CSF at different gestational and postnatal ages. Third, lumbar punctures were not performed in all cases of sepsis or clinical instability because repeated lumbar puncture was not part of routine care in every case of meningitis if clinical signs improved. Fourth, computed tomography and magnetic resonance imaging were not likely to be performed in cases of meningitis unless the patients had complications. Fifth, there was no long term neurodevelopmental assessment or regular follow-up schedule.

In summary, the overall prevalence of culture-proven meningitis at the NICU, Songklanagarind Hospital, Songkhla during 1991-2014 was 0.37/1,000 live births with a case fatality rate of 21.7%. Lower GA, BW, actual weight, and fewer cases of previous neurological surgery were manifested in meningitis cases during 2003-2014. *A. baumannii* was the most common causative organism and cause of death. Thus, broad-spectrum empirical antimicrobials should be considered in cases of severe meningitis or septic shock as well as 48 hours after birth in areas with high prevalence of MDR bacteria.

ACKNOWLEDGEMENTS

The study was supported by the Faculty of Medicine, Prince of Songkla University. The authors thank Mr Glenn Shingledecker, Office of International Affairs, Prince of Songkla University for editing and assisting with the English of the manuscript.

CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

REFERENCES

Antachopoulos C, Karvanen M, Iosifidis E, *et al*. Serum and cerebrospinal fluid levels of colistin in pediatric patients. *Antimicrob Agents Chemother* 2010; 54: 3985-7.

Bedford H, de Louvois J, Halket S, Peckham C, Hurley R, Harvey D. Meningitis in infancy in England and Wales: follow up at age 5 years. *BMJ* 2001; 323: 533-6.

Centers for Disease Control and Prevention (CDC), National Healthcare Safety Network (NHSN). Pneumonia (ventilator-associated [VAP] and non-ventilator-associated pneumonia [PNEU]) event. Atlanta: CDC, 2018. [Cited 2018 Feb 1]. Available from: http://www.cdc.gov/nhsn/pdfs/pscmanual/6pscvapcurrent.pdf

Chang CJ, Chang WN, Huang LT, *et al*. Neonatal bacterial meningitis in southern Taiwan. *Pediatr Neurol* 2003; 29: 288-94.

Chang B, Wada A, Hosoya M, *et al*. Characteristics of group B *Streptococcus* isolated from infants with invasive infections: a population-based study in Japan. *Jpn J Infect Dis* 2014; 67: 356-60.

Chotpitayasunondh T. Bacterial meningitis in children: etiology and clinical features, an 11-year review of 618 cases. *Southeast Asian J Trop Med Public Health* 1994; 25: 107-15.

De Bonis P, Lofrese G, Scoppettuolo G, *et al*. Intraventricular versus intravenous colistin for the treatment of extensively drug resistant *Acinetobacter baumannii* meningitis. *Eur J Neurol* 2016; 23: 68-75.

Furyk JS, Swann O, Molyneux E. Systematic review: neonatal meningitis in the developing world. *Trop Med Int Health* 2011; 16: 672-9.

Galiza EP, Heath PT. Improving the outcome of neonatal meningitis. *Curr Opin Infect Dis* 2009; 22: 229-34.

Gaschignard J, Levy C, Romain O, *et al.* Neonatal bacterial meningitis 444 cases in 7 years. *Pediatr Infect Dis J* 2011; 30: 212-7.

Heath PT, Yusoff NKN, Baker CJ. Neonatal meningitis. *Arch Dis Child* 2003; 88: 173-8.

Holt DE, Halket S, de Louvois J, Harvey D. Neonatal meningitis in England and Wales: 10 years on. *Arch Dis Child Fetal Neonatal Ed* 2001; 84: F85-9.

Hristeva L, Booy R, Bowler I, Wilkinson AR. Prospective surveillance of neonatal meningitis. *Arch Dis Child* 1993; 69: 14-8.

Kavuncuoglu S, Gursoy S, Turel O, Aldemir EY, Hosaf E. Neonatal bacterial meningitis in Turkey: epidemiology, risk factors, and prognosis. *J Infect Dev Ctries* 2013; 7: 73-81.

Magiorakos AP, Srinivasan A, Carey RB, *et al.* Multidrug-resistant, extensively drug-resistant and pandrug-resistant bacteria: an international expert proposal for interim standard definitions for acquired resistance. *Clin Microbiol Infect* 2012; 18: 268-81.

Pattarathitikul S. Incidence of childhood meningitis at Prapokklao Hospital since 2001-2011. *J Prapokklao Hosp Clin Med Educ Center* 2012; 29: 24-31.

Saleem AF, Shah MS, Shaikh AS, Mir F, Zaidi AKM. *Acinetobacter* species meningitis in children: a case series from Karachi, Pakistan. *J Infect Dev Ctries* 2011; 5: 809-14.

Searejitima A. Bacterial meningitis in children at Maharat Nakhon Ratchasima Hospital: a 5-year review. *Nakhon Ratch Med Bull* 2007; 31: 11-9.

Shane AL, Sanchez PJ, Stoll BJ. Neonatal sepsis. *Lancet* 2017; 390: 871-81.

Stevens JP, Eames M, Kent A, Halket S, Holt D, Harvey D. Long term outcome of neonatal meningitis. *Arch Dis Child Fetal Neonatal Ed* 2003; 88: F179-84.

Thatrimontrichai A, Apisarnthanarak A, Chanvitan P, Janjindamai W, Dissaneevate S, Maneenil G. Risk factors and outcomes of carbapenem-resistant *Acinetobacter baumannii* bacteremia in neonatal intensive care unit: a case-case-control study. *Pediatr Infect Dis J* 2013; 32: 140-5.

Thatrimontrichai A, Chanvitan P, Janjindamai W, Dissaneevate S, Jefferies A, Shah V. Trends in neonatal sepsis in a neonatal intensive care unit in Thailand before and after construction of a new facility. *Asian Biomed* 2014; 8: 771-8.

Thatrimontrichai A, Khunnarakpong N, Tantichanthakarun P, *et al.* Neonatal group B *Streptococcus* sepsis: a multicenter study in Thailand. *Southeast Asian J Trop Med Public Health* 2017a; 48: 1063-71.

Thatrimontrichai A, Rujeerapaiboon N, Janjindamai W, *et al*. Outcomes and risk factors of ventilator-associated pneumonia in neonates. *World J Pediatr* 2017b; 13: 328-34.

Thatrimontrichai A, Techato C, Dissaneevate S, *et al.* Risk factors and outcomes of carbapenem-resistant *Acinetobacter baumannii* ventilator-associated pneumonia in the neonate: a case-case-control study. *J Infect Chemother* 2016; 22: 444-9.

Yossuck P, Preedisripipat K. Neonatal group B *Streptococcal* infection: incidence and clinical manifestation in Siriraj Hospital. *J Med Assoc Thai* 2002; 85: S479-87.