

DEMOGRAPHIC PROFILE AND OUTCOMES OF POTENTIALLY SEPTIC PATIENTS AT BAGUIO GENERAL HOSPITAL (July 2004- June 2006)

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ABSTRACT

Sepsis is a common cause of morbidity and mortality among high risk neonates with intrauterine maternal history of infection.

Objectives: The main objective of this study is to describe all potentially septic newborns in the neonatal care unit of the Baguio General Hospital and Medical Center (BGH) including identification of the maternal risk factors and clinico-bacteriologic profile of sepsis of this study population.

Methods: This is a retrospective, descriptive study where medical records of all admitted potentially septic neonates from July 1, 2004 to June 30, 2006 were reviewed. Neonates who were preterm, asphyxiated, with congenital anomalies and with incomplete charts were excluded. Data such as demographics, maternal risk factors, and clinical course were recorded using a standardized clinical assessment form.

Results: Out of 217 subjects, 74% (204) were included in the study. 53% were males, with birth weights of 2500 to (-) 3800 grams (85.29%) and delivered via normal, spontaneous delivery (63.24%). The more common maternal risk factor identified included premature rupture of membranes (77%), non-institutional delivery (9.2%), and maternal urinary tract infection (4.2%). 85.78% of subjects had culture negative results, while 14.22% had culture positive results. Among patients with culture negative results, 22.29% developed clinical signs of sepsis such as poor suck, pneumonia, fever, shock, and thrombocytopenia. In patients with culture positive results, the most common organisms isolated were *Enterobacter aerogenes* (55%), *Acinetobacter baumannii* (14%) and *Coagulase negative staphylococcus* (14%). Among these patients, 10 % presented with meningitis, pneumonia, and poor suck. Empiric antibiotics used at the time of study were Penicillin G and an aminoglycoside. 66% of the asymptomatic patients with culture negative results had 3 days duration of treatment. 94.6% went home improved.

Conclusion: Pediatricians should have a high index of suspicion for the possibility of sepsis guided by complete perinatal history, thorough physical examination, and laboratory work-up. Even with negative blood culture results, neonates with maternal risk factors can develop signs and symptoms of sepsis; and with the emergence of new pathogens that may cause early neonatal sepsis, it is prudent to do blood culture and sensitivity and start empiric antibiotics.

INTRODUCTION

Through the years, neonatal sepsis continues to be a severe, often, life-threatening condition, despite the emergence of new antimicrobial agents, development of adjunctive therapies, and sophisticated life support facilities. Throughout the world, 1.6 million neonates die every year from sepsis.¹ Most of these deaths are in developing countries like ours. Aside from high mortality rates, sepsis is also being recognized as a cause of long term disability. In the annual statistical reports of the neonatal care unit of our hospital, sepsis is the leading cause of mortality and the second cause of morbidity after low birth weight from 2001 up to the present.

Early detection of sepsis in neonates is imperative to institute prompt management because sepsis may present a very serious threat. The objective of this study was to describe all potentially septic newborns in the neonatal care unit of the Baguio General Hospital and Medical Center (BGH) (this institution) including identification of the maternal risk factors and clinico-bacteriologic profile of sepsis of this study population.

MATERIALS AND METHODS

This study is a descriptive retrospective study conducted in the neonatal care unit of Baguio General Hospital and Medical Center—a tertiary hospital in Northern Luzon—from July 1, 2004 to June 30, 2006.

Study Population: Eligible neonates include those born to mothers with maternal risk factors which predisposed them to acquire sepsis such as: (1) prolonged rupture of membranes (>18 hours), (2) fetal distress, (3) maternal pyrexia (>38C), (4) overt infection (e.g. urinary tract infection, diarrheal or respiratory illness), (5) multiple obstetric procedures, and (6) non-institutional delivery. The neonates in the study are term (\geq 37 weeks age of gestation) and are included regardless of their birth weights.

Preterm neonates, severely asphyxiated neonates, those with congenital anomalies, and those who presented with signs and symptoms of sepsis immediately from the time of delivery were excluded from the study due to other confounding problems necessitating aggressive diagnostic tests and management. Potentially septic neonates, on whom blood culture and sensitivity were not done, were also excluded. Those who have incomplete data on their respective charts, as well as, those with missing charts, were likewise excluded.

Data Collection: The following data were collected from the patients:

1. Demographics: name, sex, age of gestation, birth weight, manner of delivery;
2. Maternal risk factors;
3. Clinical data: blood culture and sensitivity results, initial medications, number of hospital stay, neonatal outcome.

DEFINITION OF TERMS

1. *Potential sepsis* - Neonates with maternal risk factors such as: (1) prolonged rupture of membranes (>18 hours), (2) fetal distress, (3) maternal pyrexia (>38C), (4) overt infection (e.g. urinary tract infection, diarrheal or respiratory illness), (5) multiple obstetric procedures, and (6) non-institutional delivery.
2. *Clinical Sepsis* - Infants presenting with signs and symptoms of sepsis such as hypothermia/ hyperthermia, poor suck, poor activity, tachycardia, and tachypnea with negative blood culture.

RESULTS

Records showed that a total of 273 neonates were admitted as potential sepsis patients at the BGH from July 1, 2004 to June 30, 2006. There were 19 incomplete charts and 37 charts that were not retrieved from the Medical Records section. There were 13 patients on whom blood culture and sensitivity was not performed upon the discretion of the attending physician. Included in the study were

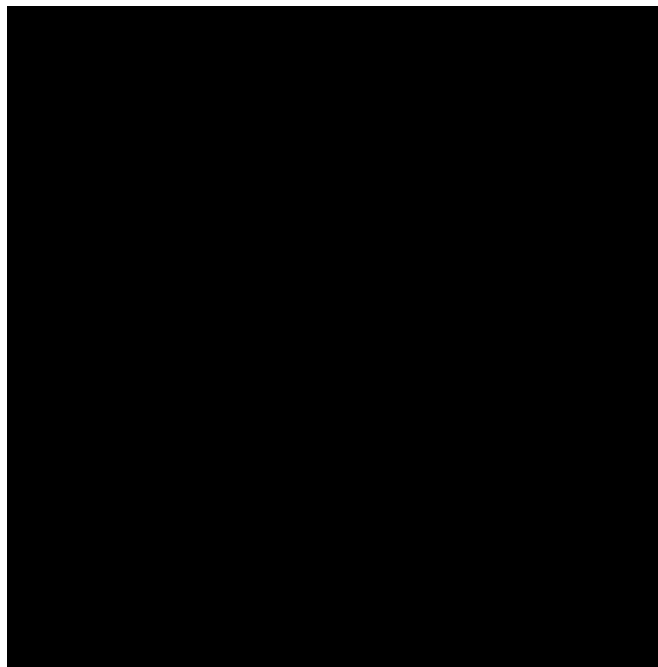
a total of 204 cases. From this population of potentially septic neonates, majority comprised of males with a total of 109 (53%) as compared to females with a total of 95 (47%).

One hundred twenty nine (63.24%) of the neonates delivered were via normal spontaneous delivery, 73 (35.78%) were via low segment cesarean section, while the rest—2 (0.98%), were via forceps delivery.

Most of the neonates (174 or 85.29%) had birth weights of 2500 to (-) 3800 grams, and 29 (14.22%) had low birth weight that ranged from 1500 to (-) 2499 grams; only (The rest,) 1 or 0.49% was (were) large for his gestational age with birth weight of >3800 grams.

Blood culture and sensitivity were (was) performed on 204 potentially septic neonates. Among whom, 175 (85.78%) had culture negative results and 29 (14.22%) were culture positive.

Figure 1. Maternal Risk Factors of Potentially Septic Infants



Among the 204 potentially septic neonates, 175 had culture negative results. 136 (77.71%) of those with culture negative results were symptom-free, and the rest (39 or 22.29%) had symptoms.

The signs and symptoms of potentially septic neonates with culture negative results presented with neonatal pyuria (20 or 51%), poor suck (8 or 20%), respiratory distress (5 or 13%), fever (4 or 10%), thrombocytopenia (1 or 3%), and shock (1 or 3%). Twenty-nine of the 204 potentially septic neonates had culture positive results.

Table 1. Culture Results of Potentially Septic Neonates in Accordance to the Different Maternal Risk Factors.

Maternal Risk	N	Culture Negative	Culture Positive
PROM	158	135 (85.44%)	23
18-23 hours	62	50 (80.65%)	(14.56%)
24-48 hours	72	62 (86.11%)	12 (19.35%)
49- 72 hours	4	4 (100%)	10 (13.89%)
>72 hours	20	19 (95%)	0 1(5%)
Non-institutional delivery	19	16 (84.21%)	3 (15.79%)
Maternal UTI	9	9 (100%)	0
Multiple Risk Factors	8	8 (100%)	0
Maternal Fever	5	3 (60%)	2 (40%)
Thickly meconium stained amniotic fluid	3	3 (100%)	0
Maternal cough and fever	1	1 (100%)	0
Maternal genital wart	1	0	1(100%)

The organisms isolated included 16 (55%) *Enterobacter aerogenes*, 4 (14%) *Acinetobacter baumannii*, 4 (14%) Coagulase negative staphylococcus, 2 (7%) *Enterobacter gergoviae*, 1 (3%) Anaerobic gram negative cocci, 1 (3%) *Klebsiella pneumoniae*, and 1 (3%) *Enterobacter cloacae*. All organisms isolated were considered to be significant, since growth occurred within 72 hours and were isolated aseptically from 2 sites.

Enterobacter aerogenes (11 or 41.2%), *Acinetobacter baumannii* (4 or 13.8%), and Coagulase Negative *Staphylococcus* (4 or 13.8%) were the most common isolates noted in potentially septic neonates with premature rupture of membranes as a maternal risk factor. In other maternal risk factors such as

maternal fever and non-institutional delivery, *Enterobacter aerogenes* was the most common isolate.

Table 2-4 shows the in-vitro antibiotic sensitivity pattern of the different microorganisms isolated.

Table 2. Sensitivity Pattern of *Enterobacter aerogenes*

Antibiotic	No. Of Isolates Tested	Sensitive (%)	Resistant (%)
Amikacin	14	13 (93%)	1 (7%)
Ampicillin	12	0	12 (100%)
Ampicillin-Sulbactam	4	0	4 (100%)
Cefepime	15	15 (100%)	0
Cefotaxime	13	13 (100%)	0
Cefoxitin	2	0	2 (100%)
Ceftazidime	14	14 (100%)	0
Ceftriaxone	12	12 (100%)	0
Gentamicin	11	11 (100%)	0
Meropenem	13	13 (100%)	0
Netilmycin	13	13 (100%)	0
Pen G Na	1	1 (100%)	0
Piperacillin	7	7 (100%)	0
Piperacillin-Tazobactam	12	12 (100%)	0
Ticarcillin	2	0	2 (100%)

Table 3. Sensitivity Pattern of Coagulase negative staphylococcus.

ANTIBIOTIC	No ISOLATES TESTED	SENSITIVE (%)	RESISTANT (%)
Cefoxitin	2	2 (100%)	0
Ciprofloxacin	4	3 (75%)	1 (25%)
Clindamycin	3	2 (67%)	1 (33%)
Gentamicin	1	0	1 (100%)
Oxacillin	4	2 (50%)	2 (50%)
Pen G Na	1	0	1 (100%)
Vancomycin	4	4 (100%)	0

Table 3. Sensitivity Pattern of *Acinetobacter baumannii*.

Antibiotic	No. Of Isolates Tested	Sensitive (%)	Resistant (%)
Amikacin	3	3 (100%)	0
Ampicillin	1	0	1 (100%)
Cefepime	4	4 (100%)	0
Cefotaxime	1	1 (100%)	0
Ceftazidime	3	3 (100%)	0
Ceftriaxone	1	1 (100%)	0
Ciprofloxacin	4	4 (100%)	0
Gentamicin	3	3 (100%)	0
Meropenem	3	3 (100%)	0
Piperacillin	1	1 (100%)	0
Piperacillin-Tazobactam	2	2 (100%)	0

Majority (200 or 98%) of the potentially septic neonates was started with a combination of Penicillin G Na 50,000 u/kg/dose every 12 hours and Amikacin 15 mg/kg/dose once a day, which was the standard empiric therapy in the neonatal care unit at the time of the study. One patient (0.5%) was started with a combination of Ampicillin 50 mg/kg/dose every 12 hours and Amikacin 15 mg/kg/dose once a day, while 3 (1.5%) were started with a combination of Penicillin G Na 50,000 u/kg/dose every 12 hours and Netilmycin 5 mg/kg/dose once a day. Antimicrobial agents were shifted according to the in-vitro antibiotic sensitivity pattern of the different microorganisms isolated.

Treatment duration varied from 1 day to 5 days in asymptomatic potentially septic neonates with negative blood culture results. Majority were (are) discharged after 3 days. Those with culture negative results but presented with signs and symptoms, as well as, those with culture positive results with or without symptoms were treated longer. Majority (193 or 94.6%) of the admitted potentially septic neonates, whether with culture negative or culture positive results, or with or without clinical manifestations, were discharged improved. Some (8 or 3.92%) went

home against medical advice. (2 or 0.98%) Two or 0.98% transferred to other hospitals. One (0.5%) died of sepsis.

DISCUSSION

Certain maternal risk factors predispose a neonate to acquire sepsis. In our institution, the identified risk factors include premature rupture of membranes (PROM), non-institutional delivery, maternal urinary tract infection, maternal fever, thickly meconium stained amniotic fluid, maternal cough, genital wart and combinations thereof, as comparable to the study done by Betty, et. al.

Among these maternal risk factors, premature rupture of membranes occurs in approximately 10% of pregnancies. In the study, the most common maternal risk factor among the neonates admitted for potential sepsis was premature rupture of membranes. At term, infection remains the most serious complication associated with PROM for the neonate. In the study, a number of neonates born to mothers with premature rupture of membranes had *Enterobacter aerogenes*, *Acinetobacter baumannii*, and Coagulase negative *staphylococcus* isolated from their blood.

The risk of chorioamnionitis with term PROM has been reported to be less than 10% and would increase to 24% after 24 hours of PROM.¹⁶ In the clinical practice guidelines of the Department of Pediatrics, it states that PROM ≥ 18 hours is significantly related to sepsis. It further states that PROM increases neonatal morbidity by 2% within 23 hours, 7% at 24 to 48 hours, and 11% at 48 to 72 hours. However, this was not reflected in this study. There was no direct relationship between the duration of PROM to the development of sepsis or bacteremia. Only 18.46% of the potentially septic neonates with PROM for 18 to 23 hours had positive culture growths as compared to 13.33% with PROM of 24 to 48 hours and 4.35% with PROM of > 72 hours.

Early-onset, sepsis syndrome is associated with acquisition of microorganisms from the mother. The microorganisms most commonly associated with early-onset infection include group B *Streptococcus* (GBS), *Escherichia coli*, and *Listeria monocytogenes*.¹⁷ In the study, the neonates who were previously admitted as potential sepsis and who had positive culture growth reflected different results. The 3 most common isolated organisms include *Enterobacter aerogenes*, *Acinetobacter baumannii*, and Coagulase negative *staphylococcus*.

In the study of Betty,¹³ et. al. and the report of the National Neonatal Perinatal Database,¹⁴ pneumonia was the most common presentation of early-onset sepsis. Other comorbidities cited in the study of Betty, et. al. included shock, metabolic acidosis, and meningitis. The neonates in the study, presented with asymptomatic neonatal pyuria, poor suck, pneumonia, fever, thrombocytopenia, meningitis and shock.

Standard empiric antibiotic regimen consist of a combination therapy usually of Penicillin G Na and an aminoglycoside to cover for the most common etiologic agents of early-onset neonatal sepsis. This regimen should be re-examined as to its appropriateness with present data and the emergence of new pathogens causing early-onset neonatal sepsis. Thus, it is essential to do a blood culture and sensitivity determination of appropriateness of the any regimen which was empirically started.

The prognosis of admitted potentially septic neonates is good if diagnostic tests are done at the right time, and prompt treatment is initiated.

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