

A CROSS-SECTIONAL ANALYSIS OF NEONATAL BACTEREMIA IN THE NEONATAL INTENSIVE CARE UNIT OF THE PHILIPPINE GENERAL HOSPITAL FROM JULY TO DECEMBER 2006

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KEYWORDS

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ABSTRACT

The Philippine General Hospital (PGH) has the most number of high-risk infant admissions locally. Neonatal bacteremia and sepsis are the perennial problems encountered. Previous researches may not be reflective of the current situation in the Neonatal Intensive Care Unit (NICU) of PGH, thus an updated study on neonatal bacteremia becomes important.

Objectives: This study was performed to describe the clinical profile of neonates born with positive blood cultures together with the new criteria for sepsis as defined by the 2001 International Pediatric Consensus Conference at PGH from July to December 2006.

Methods: A prospective chart review of all neonates born with positive blood cultures at UP-PGH from July 1 to December 31, 2006 was performed. Demographic, clinical, and laboratory data were then analyzed.

Results: Out of 3,870 live births, 103 (2.6%) patients with positive blood cultures fulfilled the criteria of sepsis. Mothers were around 20 to 25 years of age comprising 35 (34%), less than half had prenatal check-ups and more than 2/3 had not maternal immunizations. Fifty-eight (56%) of the neonates were males, 68 were premature (66%), 76 were appropriate for gestational age (74%), and 37 were of low birth weight (36%). Most patients (62 or 60%) developed sepsis within the first 3 days of admission, while 65 (63%) patients had pneumonia. The most common organisms isolated were *Pseudomonas putida* (50 or 49%), *Burkholderia mallei* (15 or 15%) and *Burkholderia cepacia* (8 or 8%). The organisms were sensitive Cefotaxime, Cefepime and Piperacillin-Tazobactam. Of 103 subjects, 58 or 56% fulfilled the criteria for systemic inflammatory response syndrome (SIRS) for sepsis. Multivariate analysis showed that those with SIRS were 4.89 times more likely to die than those without SIRS.

Conclusion: Sepsis usually develops among neonates in less than 72 hours after their delivery at PGH. The neonates who were prone to develop sepsis were those who are male, premature, appropriate for gestational age, and of low birth weight. The organisms that predominate in PGH are usually gram-negative pathogens. The number of hospital-acquired infection is significant. SIRS could be an important prognostic factor in affecting outcome and may aid significantly in the proper diagnosis of sepsis in newborns.

INTRODUCTION

Despite several major contributors for neonatal mortality, which include respiratory failure associated with prematurity, perinatal asphyxia, and congenital malformations, neonatal sepsis continues to be a major source of morbidity and mortality in newborn infants in the developing world.

At PGH, a premier tertiary government hospital in the country, newborn deliveries averaged around 7,051 in 2004 to 7,830 in 2005. But despite the advent of enhanced knowledge in innovative technologies in newborn care and the introduction of new broad-spectrum antibiotics, neonatal sepsis remains the leading cause of mortality with sepsis case fatality rates of 21% in 2004 and 28.6% in 2005.¹

Various definition of neonatal sepsis can be found in different literatures but a standard definition was formulated by the International Pediatric Consensus Conference in 2001. Neonatal sepsis in the revised definition is described as systemic inflammatory response syndrome in the presence of or as a result of suspected or proven infection in a neonate.² This new definition was utilized in this research to clearly delineate suspected septic neonates from confirmed cases of neonatal septicemia.

Several studies show varying incidence of neonatal sepsis in their localities. A study by Salise-Oncog³ in a hospital in Bohol showed 15% culture-positivity rate out of 1,538 infants diagnosed with neonatal sepsis from 1998 to 2002. Common pathogens isolated were non-fermenting organisms (37.7%), coagulase-negative staphylococcus (24%), *Enterobacter* species (7.4%), *Klebsiella* species (6.9%), *Staphylococcus aureus* (5.7%), *Escherichia coli* (5.2%), and *Pseudomonas aeruginosa* (4.8%). Majority of these organisms were resistant to Ampicillin. A survey on blood cultures done on small gestational term neonates delivered at Davao Medical Center in 1998 by Jesswani⁴ showed 31.6% to have proven sepsis. Microorganisms isolated were *Staphylococcus*

epidermidis (59.3%), *Staphylococcus saprophyticus* (18.5%), *Acinetobacter* (11.1%), *Enterobacter cloacae* (3.7%), and *Streptococcus viridians* (3.7%).

Other researches by local authors in the National Capital Region also note the emergence of gram-negative septicemia in their surveys. A retrospective study done by Sugiarto⁵ showed gram-negative pathogens as the most common isolates with increased resistance of the organisms to aminoglycosides, cephalosporins, and extended spectrum penicillins. Logronio-Reyes⁶ et al in a study at the Philippine Children's Medical Center in 2001 showed *Burkholderia cepacia*, *Candida albicans*, *Klebsiella pneumonia*, and *Pseudomonas aeruginosa* as the most common organisms isolated.

At PGH, a study done by Fabre⁷ in 1999 showed the predominant organisms isolated in the NICU were *Enterobacter* species, *Candida*, and *Pseudomonas* species. Based on the sensitivity patterns, the antibiotics which most of the top isolates were susceptible to included Amikacin, Piperacillin-Tazobactam, Imipenem, and Ciprofloxacin. Subsequent surveillance of the Section of Infectious and Tropical Disease in 2005 showed *Enterobacter cloacae*, *Acinetobacter baumannii*, and *Staphylococcus epidermidis* as the top isolates with most organisms sensitive to most carbapenems and fourth generation cephalosporins, like Cefepime.⁸

OBJECTIVES

The aim of this study was to describe the clinical profile of neonates who were with positive blood cultures and with criteria for sepsis as defined by the 2001 International Pediatric Consensus Conference and admitted at the NICU of PGH from July to December 2006.

MATERIALS AND METHODS

Study Design

A prospective chart review of all neonates born at UP-PGH and admitted at the NICU was performed from July 1 to December 31, 2006.

Student Population

We conducted a detailed review of the medical charts of all neonates born at PGH and admitted at the NICU. Inclusion criteria are the following:

1. Neonates with positive blood cultures;
2. Neonates who present clinically with any criteria for sepsis defined under the 2001 International Pediatric Consensus Conference on sepsis.

Data Collection

The following information were collected from each of the patients, who were included in the study: maternal factors (age, prenatal check-ups, immunization, and history of infections), neonatal factors (sex, birth weight, pediatric aging, age of gestation), clinical manifestations, laboratory findings (blood culture and sensitivity and time taken, white blood cell count), radiologic data, and outcome and presence of neurologic and medical sequelae

Definition of Terms

The World Health Organization (WHO)⁹ has defined infants who were <37 weeks age of gestation or less than 259 completed days, irrespective of weight at birth, as Preterm Neonates; those with equal to or greater than 37 weeks and equal to or not more than 42 weeks (259 to 294 days), irrespective of weight at birth, as Term Neonates; and those greater than 42 weeks or equal to or greater than 259 days, irrespective of weight at birth, as Post-term Neonates. The pediatric aging (PA) was determined using the Dubowitz Scoring System.¹⁰

All neonates were grouped according to categories of birth weight – gestational age comparisons: appropriate for gestational age (AGA), small for gestational age (SGA), or large for gestational age (LGA). Graphs and tables of the normal distribution of birth weights over the latter part of gestation were used to classify each birth. Neonates whose birth weight was less than 10th percentile or greater than 90th percentile for their population were classified as SGA or LGA, respectively.

Birth weight classification was defined according to the Standards of Newborn Care of the Philippine Pediatric Society:¹¹ Low Birth Weight Neonate is defined as any neonate, regardless of gestational age, whose weight at birth is less than 2500 grams; Very Low Birth Weight (VLBW) Neonate is any neonate, regardless of gestational age, whose weight at birth is 1000 to 1500 grams; and Extremely Low Birth Weight (ELBW) Neonate is any neonate, regardless of gestational age, whose birth weight is < 1000 grams.

Maternal fever was defined as an oral temperature $\geq 38^{\circ}\text{C}$ in the absence of clinical dehydration or focal infection like urinary tract infection, pneumonia, and upper respiratory tract infection.¹² Premature rupture of membranes was defined as rupture of membranes prior to onset of labor beyond 16 hours.

Neonatal sepsis as defined by the 2001 International Pediatric Sepsis Consensus Conference is as follows:²

A. Systemic inflammatory response syndrome (SIRS)

The presence of at least two of the following four criteria, one of which must be abnormal temperature or leukocyte count:

1. Core temperature of $>38.5^{\circ}\text{C}$ or $<36^{\circ}\text{C}$;
2. Tachycardia, defined as a mean heart rate >2 SD above normal for age in the absence of external stimulus, chronic drugs, or painful stimuli; or otherwise unexplained persistent elevation over a 0.5- to 4-hr time period OR for children <1 yr old: bradycardia, defined as a mean heart rate <10 th percentile for age in the absence of external vagal stimulus, β -blocker drugs, or congenital heart disease; or otherwise unexplained persistent depression over a 0.5-hr time period;
3. Mean respiratory rate >2 SD above normal for age or mechanical ventilation for an acute process not related to underlying neuromuscular

disease or the receipt of general anesthesia;

4. Leukocyte count elevated or depressed for age (not secondary to chemotherapy-induced leukopenia) or >10% immature neutrophils.

B. Infection

A suspected or proven (by positive culture, tissue stain, or polymerase chain reaction test) infection caused by any pathogen or a clinical syndrome associated with a high probability of infection. Evidence of infection includes positive findings on clinical exam, imaging, or laboratory tests (e.g., white blood cells in a normally sterile body fluid, perforated viscus, and chest radiograph consistent with pneumonia, petechial or purpuric rash, or purpura fulminans).

C. Sepsis

Systemic Inflammatory Response Syndrome (SIRS) in the presence of or as a result of suspected or proven infection.

D. Severe sepsis

Sepsis plus one of the following: cardiovascular organ dysfunction or acute respiratory distress syndrome, or two or more other organ dysfunctions.

E. Septic shock

Sepsis and cardiovascular organ dysfunction.

Blood Culture

Blood culture incubation in PGH used the BacT/Alert System. This is an automated patented colorimetric sensor-and-detection technology developed by BioMerieux.

STATISTICAL ANALYSIS

Descriptive statistics using frequency data, percentage, mean, and standard deviation were used to evaluate demographic, maternal and neonatal risk factors. Test of association such as T-test, Chi-square and Fischer's Exact tests, bivariate analysis, and multiple logistic regression were done to determine which of the considered factors were significantly associated with neonatal sepsis.

RESULTS

Study Population

Out of the 3,870 total live births admitted at the NICU of PGH during the study (July 1 to December 31, 2006), 103 (2.6%) patients with positive blood cultures fulfilled the criteria for neonatal sepsis as defined by the 2001 International Pediatric Sepsis Consensus Conference. 58 (56%) of these neonates were males, while 45 (44%) were females.

Maternal Profile & Factors

Most mothers with infants admitted at the NICU of PGH were aged 20 to 25 years old, comprising 35 (34%) of the total population. 15 to 20 year old mothers were 13 (13%), and the 40 to 45 year olds were around 5 (5%). Mothers with prenatal check-ups at their local health units more than 5 times compromised about 46 (45%). Only 13 (13%) did not have prenatal check-up. Most mothers, also, did not have maternal immunizations. Maternal risk factors associated with sepsis were noted in 17% of infants. The presence of maternal fever and urinary tract infection diagnosed within 3 months of delivery both accounted for only 7 (7%) of the total admissions.

Neonatal Factors

Neonates diagnosed to have sepsis were usually grouped under the low birth weight category with a total of 37 (36%) admissions, followed by the very low birth weight with a total of 35 (34%), and lastly by the extremely low birth weight with a total of 7 (7%). Most, as described by Table 3, are premature neonates comprising about more than half of the total population with a total of 68 (66%). A greater number of neonates (76 or 74%) surveyed were appropriate for gestational age: 8 (8%) of these neonates were intubated for respiratory support, while no infant underwent catheterization while admitted. More than half of the neonates (58 or 56%) who developed septicemia were delivered via caesarian section, while 45 (44%) were delivered normally.

Table 1. Maternal profile and factors predisposing to sepsis.

	N=103 (%)
AGE OF MOTHER	
15 – 20 years	13 (13%)
21 – 25 years	35 (34%)
26 – 30 years	21 (20%)
31 – 35 years	19 (18%)
36 – 40 years	10 (10%)
41 – 45 years	5 (5%)
MATERNAL RISK FACTORS	
A. NUMBER OF PRENATAL VISITS	
1 – 5 times	44 (43%)
More than 5 times	46 (45%)
None	13 (13%)
B. MATERNAL IMMUNIZATION	
Tetanus	24 (23%)
Others	3 (3%)
None	76 (74%)
C. OTHER CONDITIONS	
PROM	4 (3%)
Maternal Fever	7 (7%)
UTI within 3 months	7 (7%)

Table 2. Neonatal factors predisposing to sepsis.

	N = 103 (%)
A. BIRTHWEIGHT	
Low Birth Weight (1.5 -2.5 kg)	37 (36%)
Very Low Birth weight (1.0 – 1.5 kg)	35 (34%)
Extremely Low Birth Weight (< 1.0 kg)	7 (7%)
Normal	24 (23%)
B. PEDIATRIC AGING	
Preterm (<37 weeks)	68 (66%)
Term (37 to 42 weeks)	35 (34%)
Postterm (> 42 weeks)	0
C. GESTATIONAL AGE	
Small for Gestational Age (SGA)	22 (21%)
Appropriate for Gestational Age (AGA)	76 (74%)
Large for Gestational Age (LGA)	5 (5%)
D. MANNER OF DELIVERY	
Spontaneous Vaginal Delivery	45 (44%)
Caesarian Delivery	58 (56%)
C.OTHER CONDITIONS	
Intubation	8 (8%)
Central Catheterization	0

Clinical Manifestations

Table 3 shows that the organ most involved among subjects with confirmed blood cultures was the lung, with pneumonia 65 (63%) as the most common condition. Necrotizing colitis was present in 8 (7%) subjects. There were no cases of meningitis, cellulites, or those with other underlying structures.

Table 3. Organ Involvement in Neonates with confirmed septicemia

	N=103 (%)
Pneumonia	65 (63%)
Necrotizing enterocolitis	8 (7%)
Meningitis	0
Skin and Underlying structures	0

Table 4. Description of the Systemic Inflammatory Response (SIR) syndrome In Neonates with confirmed Sepsis.

	N =58	Percent (%)
CORE TEMPERATURE		
>38.5	2	4
<36.0	6	10
Normal	50	86
HEART RATE		
Tachycardia	7	12
Bradycardia	27	47
Normal	24	41
RESPIRATORY RATE		
Mean RR > 2SD above normal for age	14	24
Mechanical ventilation	33	57
Normal	11	19
WHITE BLOOD CELL COUNT		
Elevated	8	15
Depressed for age	24	41
>10% immature neutrophils	10	22
Normal	10	22

Systemic Inflammatory Response Syndrome (SIRS)

In Table 4, out of 103 subjects, 58 or 56% fulfilled the criteria for SIRS. In 81% of the subjects with SIRS, respiratory rate was abnormal and 57% needed mechanical ventilation. The next most common manifestation of SIRS was a deranged WBC

count, present in 78% of the subjects, with depressed count for age as the most common abnormal finding. Abnormal heart rate was present in 59% of the subjects. Bradycardia at 47% was more common than tachycardia at 12%, respectively. Core temperature was also normal in 86% of subjects.

Onset of Infection

The majority of neonates (62 or 60%) admitted at the NICU developed sepsis within the first 3 days of admission, while 41 or 40% developed infection after more than 3 days of hospital stay.

Pathogen Distribution and Antibiotic Sensitivity

The most common organism isolated was *Pseudomonas putida*, which was found in nearly half of the subjects (50 or 49%). This was followed by *Burkholderia mallei* with 15 (15%) subjects and *Burkholderia cepacia* with 8 (8%) subjects. The following were isolated in 5 subjects each: *Burkholderia pseudomallei*, *Klebsiella pneumoniae*, and MRSE. *Alkaligenes fecalis* was isolated in 4 subjects, *Pseudomonas aeruginosa* in 2 subjects. The following were isolated in one subject each: *Klebsiella ozanae* and *rhinoscleromatis*, *Enterobacter cloacae*, *Enterococcus faecium*, and *Candida* species. Sensitivity patterns of the top isolates cultured showed *Pseudomonas putida* to be susceptible to Ceftazidime (100%) and Piperacillin-Tazobactam (80%) with increased resistance rates to Meropenem (42%), Ciprofloxacin (67%), and Imipenem (77%). *Burkholderia mallei* showed susceptibility to Ceftazidime (90%), while *Burkholderia cepacia* is sensitive to Cefepime (100%) and Piperacillin-Tazobactam (100%). No sensitivity patterns were done for the *Candida* species isolated in 1 patient.

Table 5. Blood Culture and Sensitivity Pattern.

Antibiotic	No. of Isolates Tested	No. of Isolates Sensitive (%)	No. of Isolates Resistant (%)
<i>Acinetobacter baumannii</i> (n= 5).			
Gentamicin	1	0	1 (100%)
Amikacin	3	0	3 (100%)
Ampicillin	5	1 (20%)	4 (80%)
Cefuroxime	2	1 (1%)	1 (50%)
Ceftazidime	4	1 (25%)	3 (75%)
Ceftriaxone	2	1 (50%)	1 (50%)
Cefepime	4	1 (25%)	3 (75%)
Ciprofloxacin	2	0	2 (100%)
Piper Tazo	5	2 (40%)	3 (60%)
Meropenem	2	1 (50%)	1 (50%)
Imipenem	2	0	2 (100%)
<i>Burkholderia cepacia</i> (n= 8)			
Gentamicin	1	0	1 (100%)
Amikacin	2	0	2 (100%)
Cefuroxime	1	1(100%)	0
Ceftazidime	5	5 (100%)	0
Ceftriaxone	1	1 (100%)	0
Cefepime	4	4 (100%)	0
Ciprofloxacin	1	0	1 (100%)
Piper Tazo	3	3 (100%)	0
Meropenem	4	3 (75%)	1 (25%)
Imipenem	4	2 (50%)	2 (50%)
<i>Burkholderia cepacia</i> (n= 8)			
Amikacin	3	0	3 (100%)
Ampicillin	6	1 (16%)	5 (83%)
Ceftazidime	10	9 (90%)	1 (10%)
Ceftriaxone	4	3 (75%)	1 (25%)
Cefepime	10	10 (100%)	0
Ciprofloxacin	8	4 (50%)	4 (50%)
Piper Tazo	10	10 (100%)	0
Meropenem	5	2 (40%)	3 (60%)
Imipenem	8	0	8 (100%)
<i>Burkholderia pseudomallei</i> (n=5).			
Netilmicin	1	0	1 (100%)
Ampicillin	1	0	1 (100%)
Ceftazidime	1	1 (100%)	0
Cefepime	2	1 (50%)	1 (50%)
Ciprofloxacin	1	0	1 (100%)
Piper Tazo	4	4 (100%)	0
Meropenem	2	2 (100%)	0
<i>Klebsiella pneumoniae</i> (n=5)			
Tobramycin	1	1	0
Netilmicin	1	1	0
Amikacin	4	1	3 (75%)
Ampicillin	5	0	5 (100%)
Cefazolin	2	1 (50%)	1 (50%)
Cefuroxime	3	1 (33%)	2 (66%)
Cefotaxime	1	0	1 (100%)
Ceftazidime	2	0	2 (100%)
Ceftriaxone	4	1 (25%)	3 (75%)
Cefepime	3	0	3 (100%)
Piper Tazo	4	2 (50%)	2 (50%)
Imipenem	1	1 (100%)	0

Antibiotic	No. of Isolates Tested	No. of Isolates Sensitive (%)	No. of Isolates Resistant (%)
<i>Pseudomonas putida</i> (n=50)			
Gentamicin	7	0	7 (100%)
Tobramycin	2	0	2 (100%)
Netilmicin	2	0	2 (100%)
Amikacin	22	0	22 (100%)
Ampicillin	17	0	17 (100%)
Cefuroxime	6	2 (33%)	4 (67%)
Cefotaxime	1	0	1 (100%)
Ceftazidime	16	16 (100%)	0
Ceftriaxone	19	15 (79%)	4 (21%)
Cefepime	25	21 (84%)	4 (16%)
Ciprofloxacin	18	6 (33%)	12 (67%)
Piper Tazo	20	16 (80%)	4 (20%)
Meropenem	12	8 (67%)	5 (42%)
Imipenem	22	5 (23%)	17 (77%)
Cotrimoxazole	24	21 (88%)	3 (22%)
MRSE (n=5)			
Clindamycin	1	0	1(100%)
Oxacillin	2	0	2(100%)
Vancomycin	3	3 (100%)	0

Table 6. Outcome of hospitalization in Neonates with Confirmed Sepsis.

OUTCOME	No of patients N=103	Percent (%)
SURVIVED	78	76%
No neurologic/ medical sequelae	76	97%
With neurological/ medical sequelae	2	3%
DIED	25	24%

Outcome of Hospitalization

The mortality rate from confirmed neonatal sepsis cases was 24%; 76% survived with majority of those admitted without medical and neurological sequelae on discharge. Results of the bivariate analysis of factors affecting outcome in Table 7 shows that only the number of prenatal check-up, weight classification, and presence of SIRS significantly affected outcome with ($p < 0.05$).

Factors which showed significance on bivariate analysis were then entered into a logistic regression model to determine independent factors affecting outcome. Table 8 shows that only SIRS was significant, while weight was borderline significant. Those with

SIRS were 4.89 times more likely to die than those without SIRS.

Table 7. Factors Affecting Outcome: Bivariate analysis.

	Survived	Died	P value
PRENATAL CHECK-UP			
Mean	4.76	3.36	0.049
SD	3.28	2.90	
AGE OF GESTATION			
Mean	34.26	32.64	0.085
SD	3.54	4.09	
PNEUMONIA			
Present	48	17	0.560
Absent	30	8	
NECROTIZING ENTEROCOLITIS			
Present	7	1	0.419
Absent	71	24	
WEIGHT CLASSIFICATION			
Normal - LBW	51	10	0.025
VLBW - ELBW	27	15	
SIRS			
Present	37	21	0.0013
Absent	41	4	

DISCUSSION

From the surveillance conducted during the study period, only 103 cases of the 3,870 deliveries at PGH developed sepsis according to the revised definition of the International Pediatric Sepsis Consensus Conference. This may appear minimal in terms of percentage but 2.6% cannot also be totally discounted. The figures may also suggest that the actual sepsis rate of the hospital may be lower than what is actually perceived, if the new definitions of sepsis are to be followed. This can bear significance in the overall diagnosis and in turn widespread use of resources like antibiotics, which may not be necessary in most cases of neonates admitted at this institution.

Statistics shows that more males (58 or 56%) developed sepsis than females (45 or 44%), which supports most studies on this case. The reasons behind this male predominance are generally unknown but may be related to sex-linked factors in host susceptibility.¹² Some studies cite the male disadvantage to a gene

Table 8. Factors Affecting Outcome: Multivariate analysis.

Predictor	Coefficient	Standard Deviation	Z	P	Odds Ratio	95% Confidence Interval (Lower)	95% Confidence Interval (Upper)
Weight	0.9818	0.5047	1.95	0.052	2.67	0.99	7.18
Prenatal Check-ups	-0.13307	0.09457	-1.41	0.159	0.88	0.73	1.05
SIRS	1.5873	0.6057	2.62	0.009	4.89	1.49	16.03

locus in the X chromosome which is involved in the synthesis of immunoglobulin.¹³

Neonatal septicemia has been classified as either early onset or late onset. Infections that manifest early in the first week of life are usually attributable to microorganisms transmitted from mother to infant and have an epidemiology different from those of infections acquired later in the neonatal period.¹⁴ Several studies^{15, 16, 17, 18, 19} define early onset and late onset within 24, 48, 72 hours and < 1 week of life. A study by Gotoff showed that although term early onset sepsis has been used to refer to neonatal infections occurring as late as the 1st week of life, it should be restricted to those infections with a perinatal pathogenesis; the usual onset of which occurs within 72 hours.⁹ This study used 72 hours as cut-off. Data gathered showed that a greater majority of neonates (n= 62) admitted at the NICU developed sepsis within <72 hours of admission, while (n=41) or 40% developed infection > 72 hours of hospital stay. Neonates diagnosed to have sepsis were usually grouped under the low birth weight category with a total of 37 (36%) admissions, followed by the very low birth weight with 35 (34%) admissions, and extremely low birth weight with 7 (7%) admissions. Most (68 or 66%) were premature neonates comprising about more than half of the total population. 76 (74%) infants admitted in the nursery, who developed sepsis, were appropriate for gestational age. This is contrary to the data of Christo²⁰ and the local data gathered by Jesswani⁴, which showed that SGA infants were more likely to develop sepsis than neonates who were appropriate for gestational age (AGA). The susceptibility to infection of infants, who are small for gestational age, can

be attributed to their depressed immune system. Low C3 values have been found in these infants contributing to impaired polymorphonuclear leucocytic chemotaxis and bacteria capacity.²¹

Data shows that more than half of the neonates who developed septicemia 58 (56%) were delivered via caesarian section, while 45 (44%) were delivered normally. These figures contradict the findings of Stoll, et. al. that babies delivered vaginally are significantly more likely to have early onset sepsis than those born by caesarian section.¹³ This may be attributed to the fact that those delivered vaginally may more likely be contaminated with vaginal flora during labor and delivery. The different observations in this institution may be due to the conditions of the neonates which warranted a caesarian delivery which may have put them at high risk for sepsis.

Most mothers with infants admitted at the NICU of PGH were between 20 to 25 years of age comprising 35 (34%) of the total population. Among those surveyed, prenatal check-ups done were usually more than 5 times in 46 mothers (45%). Significant to note is that most mothers who did not have maternal immunizations (76 or 73%), indicating a need for more aggressive educational promotion by local health units on this matter of health education.

The infant is usually protected from infection by intact membranes, but if ruptured prematurely, ascending (vaginal) infection usually occurs. The longer the rupture, the more likely is fetal infection; but infection does occur even with intact membranes. Data gathered in this study showed maternal factors to be associated with sepsis like premature

rupture of membranes was only noted on 4 (3%) of infants, but neonatal sepsis due to this may not be attributed to PROM alone. Also noted is the presence of maternal fever and urinary tract infection in only 7 (7%) of the infants with sepsis admitted at this institution.

The most common organism isolated was *Pseudomonas putida*, found in nearly half of the subjects (50 or 49%). This was followed by *Burkholderia mallei* (15 or 15%) and *Burkholderia cepacia* (8 or 8%). The most common organisms responsible for early onset sepsis usually reflect the predominant vaginal flora of the pregnant woman. The organisms involved usually are Group B Streptococcus, H. influenza, L. monocytogenes, S. pneumonia, and E. coli and Klebsiella species. The organisms isolated in this institution are different from the organisms usually found in early onset septicemia. A study done by Fabre⁷ et al. in at the NICU of PGH in 1999 showed that Enterobacter species, Candida, and Pseudomonas as the overall predominant organisms. Various institutions, locally, have different pathogens, but most have noted also the predominance of gram-negative bacteremia^(5, 6).

Sensitivity patterns of the top isolates cultured showed *Pseudomonas putida* to be susceptible to Ceftazidime (100%) and Piper-Tazo (80%), with increased resistance rates to Meropenem (42%), Ciprofloxacin (67%), and Imipenem (77%). *Burkholderia mallei* and *Burkholderia cepacia* show susceptibility to Ceftazidime (90%), Cefepime (100%), and the beta-lactam, Piper-Tazo (100%). Strict adherence to infection control measures, as well as, rational use of antibiotics should be practiced if alternative use of these broad-spectrum and expensive antibiotics is to be minimized and meager resources is to be conserved.

The organ most involved among subjects with confirmed blood cultures was pneumonia (65 or 63%); this is in accordance with previous studies done in this institution^(7, 22). Necrotizing colitis was present in 8 (7%) subjects. Although

this entity is strictly non-infectious in etiology, this finding can be expected since sick neonates have immature gastrointestinal tracts, which together with other factors promote the overgrowth of microorganisms.

Mortality rate from confirmed neonatal sepsis cases was 24%. Previous data taken at PGH shows sepsis fatality to be around 21% in 2004 and 28.6% in 2005.¹ The figure obtained may suggest that neonatal sepsis remains to be the leading cause of mortality among newborn infants, although, a larger number of subjects with surveillance done for a minimum period of 1 year may be better used to collate this data.

Statistics showed that out of 103 subjects, 58 or 56% fulfilled the criteria for Systemic Inflammatory Response Syndrome (SIRS). The International Pediatric Sepsis Consensus Conference² in 2001 revised the definition for sepsis in order to aid in the standardization of observational studies and evaluation of therapeutic interventions in clinical trials. SIRS as part of the criterion for sepsis was proposed by the American College of Chest Physicians and Society of Critical Care Medicine to describe the nonspecific inflammatory process occurring in adults after trauma, infection, burns, pancreatitis, and other diseases. Sepsis was defined as SIRS associated with infection. The major difference in the definition of SIRS between adults and children is that diagnosis of SIRS requires that temperature or leukocyte abnormalities be present. SIRS should not be diagnosed if a pediatric patient exhibits only elevated heart and respiratory rates. In addition, numeric values for each criterion need to be modified to account for the different physiology of children. Finally, bradycardia may be a sign of SIRS among newborns but not in older children in whom it is a near-terminal event. In this study, of the 81% of the subjects who fulfilled the criteria for SIRS, 57% had abnormal respiratory rate requiring mechanical ventilation. Deranged WBC count was present in 78% of the subjects, with depressed count for age as the most common abnormal finding. Abnormal heart

rate was present in 59% of the subjects, with bradycardia (47%) as the more common cause than tachycardia (12%). Core temperature was also normal in 86% of subjects. Results of multivariate logistic regression suggest that SIRS is an important prognostic factor affecting outcome such as mortality. It could be used significantly in the proper diagnosis of suspected neonatal cases of sepsis, but a larger sample size and the use of control subjects are recommended.

CONCLUSIONS AND RECOMMENDATIONS

Results of this study indicate that in this institution, sepsis usually develops in less than 72 hours after delivery and is usually seen in males, prematures, appropriate for gestational age and low birth weight neonates. The organisms that predominate in PGH are usually gram-negative pathogens with *Pseudomonas putida*, *Burkholderia mallei*, and *Burkholderia cepacia* as the top isolates. These organisms indicate a high probability that hospital-acquired contamination is to be considered in neonates with early onset septicemia in this institution. Most of these organisms are sensitive to Ceftazidime, Cefepime, and the beta-lactam Piper-Tazo. Strict adherence to infection-control measures, as well as, rational use of antibiotics should be practiced if the use of broad-spectrum and expensive antibiotics is to be minimized and meager resources is to be conserved.

The use of the definition of sepsis in pediatrics as proposed by the International Pediatric Sepsis Consensus Conference is recommended for future studies on neonatal sepsis in order to aid in standardization of observational studies and evaluation of therapeutic interventions in clinical trials. SIRS is an important prognostic factor in affecting outcome and could be used significantly in the proper diagnosis of septicemia in newborns. Proper diagnosis means subsequent appropriate treatment and conservation of resources. Since this study has been limited to a short duration and in the number of subjects, it

is therefore recommended that another study be done on a bigger population, with the subjects appropriately matched with a control group to determine the validity of this criterion as a sensitive indicator of sepsis in neonates.

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