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CLINICAL CORRELATION OF NEONATAL AND MATERNAL HEMATOLOGICAL PARAMETERS AS PREDICTORS OF NEONATAL SEPSIS

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ABSTRACT

Objective: To evaluate the neonatal and maternal clinical manifestations and their hematological parameters, individually and in combination, as parameters which can be used to formulate a scoring system in determining neonatal sepsis.

Design: A cross-sectional study conducted at the Neonatal Intensive Care Unit of a tertiary care teaching hospital.

Methods: The study consisted of 100 neonates admitted at Neonatal Intensive Care Unit at the UP-PGH Medical Center who were clinically suspected of sepsis at birth and within 24 hours of life. A perinatal history, clinical profile, symptoms and laboratory data were recorded in each case. The neonatal hematological parameters included were total leukocyte count, total neutrophil count, lymphocytes, immature cells, immature to total leukocyte ratio, immature to mature cells ratio, nucleated red blood cells, lymphocytes, absolute neutrophil count, platelet count, and toxic granules. The maternal hematological parameters consisted of total leukocyte count, total neutrophil count, lymphocytes and platelet count. These parameters were evaluated based on the standard reference values. A blood culture was the standard indicator for proven sepsis.

Results: There were 17 out of 100 neonates (17%) who had culture proven sepsis and they were predominantly preterm. Among the different parameters, the preterm infants, neonatal platelet count and maternal total leukocyte count were significantly associated with neonatal sepsis with *p* value of 0.047, 0.02, and 0.006 respectively. Based on these factors, a scoring system was devised to predict the probability of sepsis. A score of 3 had a 100% sensitivity and 91.3% specificity.

Conclusion: A scoring system for predicting neonatal sepsis could be obtained by correlating the clinical manifestations of the neonate and the mother together with their hematological parameters.

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Keywords: Neonatal sepsis, hematological parameters, scoring system, newborn, perinatal infection

INTRODUCTION

Sepsis neonatorum is used to describe the systemic response to infection in newborn infants. It continues to be the major cause of morbidity and mortality in the newborn.[1] Neonatal sepsis occurs in 1 to 8 cases of all live births.[2] In the Philippines, the incidence is estimated between 4 to 9 cases per 1000 live births.[3] In the Neonatal Intensive Care Unit of the University of the Philippines – Philippine General Hospital, it is estimated between 2 to 7 cases per 1000 live births with an average sepsis rate of 7%.[4]

Neonatal sepsis is categorized as early or late onset. Eighty-five percent of newborns with early onset of infection present within 24 hours, 5% present at 24-48 hours, and a smaller percentage of patients present between 48 hours and 6 days of life.[5] The susceptibility of the newborn is related to immaturity of both the cellular and humoral immune systems at birth. This feature is particularly evident in preterm neonate. Early-onset sepsis syndrome is also associated with acquisition of microorganisms from the mother through blood-borne transplacental infection of the fetus, ascending infection, and infection upon passage through an infected birth canal or exposure to infected blood at delivery.[6] Late-onset sepsis syndrome occurs at 7-90 days of life and is acquired from the care-giving environment.

The early signs of sepsis in the newborn are nonspecific. Therefore, many newborns undergo diagnostic studies and the initiation of treatment before the diagnosis has been determined. The definitive diagnosis of septicemia is made by a positive blood culture.[1] The incidence of culture proven sepsis is approximately 2 in 1000 live births. Of the 7-13% of neonates who are evaluated for sepsis, only 3-8% have culture proven sepsis. The mortality rate of untreated sepsis can be as high as 50%.[5] Thus, most clinicians believe that the hazard of untreated sepsis is too great to wait for confirmation by positive cultures. They initiate treatment while awaiting culture results.

However, due to the high cost of antibiotics, inavailability of blood cultures in some community hospitals, and the time it takes for the blood culture result to come out, several studies have examined the laboratory findings associated with sepsis. There is a lack of consensus on the essential test that would identify neonates with acute infection. In a systematic review to determine the value of diagnostic tests for bacterial infection in early life, it was reported that the accuracy of tests varies enormously and the tests are of limited value in the diagnosis of infection.[7] In another study, a combination of hematological and biochemical tests (eg. acridine orange leukocyte cytospin test, nitroblue tetrazolium and C-reactive protein) may provide a more rapid and accurate diagnosis of bacteremia than conventional microbiological methods.[8] In recent years, various investigators have evaluated some highly sensitive and specific inflammatory markers (eg. C-reactive protein, interleukin-6, interleukin-8, plasma elastase) to diagnose neonatal sepsis and shock. Although these markers are sensitive and specific, they require sophisticated and expensive kits and are therefore impractical for routine clinical work-up in a community health delivery systems, particularly in developing countries.[1]

The use of hematological parameters for determining sepsis was evaluated in different studies. There was significant heterogenicity across these studies.[9] The possible sources were population, age, subjects, methodological quality, different leukocyte indices, different cut-offs and interpretation of test results by different laboratory observers. However, these parameters remain to be rapid, economical, feasible, practically possible in all laboratories and most especially, these hematological parameters can be used as a tool in screening neonates with sepsis[1] which in turn may decrease the antibiotic usage.[10]

GENERAL OBJECTIVE

This study is designed to evaluate the neonatal and maternal clinical manifestations and their hematological parameters, individually and in combination, as parameters which can be used to formulate a scoring system in predicting the probability of neonatal sepsis.

SPECIFIC OBJECTIVES

1. To provide a rapid identification of sepsis based on complete blood count and peripheral blood smear in correlation with clinical symptoms
2. To compare neonates who are more prone to infection based on gestational age, weight, sex and manner of delivery
3. To determine whether the newborn and maternal symptoms correlate well with neonatal sepsis
4. To determine which of the newborn hematological parameters, namely: the white blood count (WBC) or total leukocyte count (TLC), total neutrophil count (TNC), lymphocytes, immature cells, immature to total neutrophil cells (I/T) ratio, immature to mature cells (I/M) ratio, absolute neutrophil count, nucleated red blood cells (NRBC), platelet count and toxic granulation, are significant in predicting sepsis
4. To determine whether the maternal white blood count, different count, and platelet count are also significant in predicting sepsis

STUDY DESIGN

This is a cross-sectional study conducted at the Neonatal Intensive Care Unit of a tertiary care teaching hospital.

METHODS

Subjects

The study consisted of 100 neonates admitted at Neonatal Intensive Care Unit (NICU) at the Philippine General Hospital from July to September 2003 who were clinically suspected of sepsis at birth and within 24 hours of life or had maternal history of infection.

Inclusion Criteria:

Neonates with respiratory distress syndrome, cyanosis, apnea, transient tachypnea, meconium aspiration syndrome, pneumonia, low Apgar score, birth asphyxia, lethargy, temperature instability, and hypoglycemia.

Neonates with maternal history of infection such as upper respiratory tract infection, pneumonia, urinary tract infection, vaginitis, premature rupture of membrane, chorioamnionitis, with or without antibiotic intake during pregnancy.

Newborn with gestational age of 30 weeks and above by pediatric aging and with a weight of more than or equal to 1000 grams.

Study Procedure

Each neonate was examined by a pediatric resident rotating in NICU or neonatology fellow who recorded the signs and symptoms of the neonate, predisposing perinatal factors and the clinical assessment of the neonate.

Initial tests performed were complete blood count, peripheral smear and blood culture. Blood samples (2 ml) were collected from the umbilical cord, peripheral

venous or arterial puncture within 24 hours of admission before initiation of antibiotic therapy.

A 0.5-1 ml of blood sample was anticoagulated with ethylene diamine tetra acetic acid. The total leukocyte count and platelet count were measured on a Coulter STKS. White blood cells were corrected for nucleated red blood cells. Peripheral blood smears were drawn on clean slides and stained by Wright's stain. A differential leukocyte count was done to obtain the total neutrophil count (TNC), immature neutrophil count (IM), including bands and stabs; and mature neutrophil count (M). Neutrophils were classified as band forms when there were no nuclear segmentation or when the width of the nucleus at any constriction was not less than one third the width at its widest portion. Band forms together with less mature cell form were classified as immature polymorphonuclear (PMN) leukocytes. Using these values, I/M and I/T ratios were computed. One hundred neutrophils were further examined for degenerative changes such as toxic granulation, Dohle bodies, and vacuolization. Toxic granulation was graded as 0 or (-) which indicated normal granulation or no toxic granules seen, (+) slight, (++) approximately 50% of neutrophils contained dark granules, (+++) very high granulation in most cells, and (++++) gross toxic granulation with the nucleus obscured by toxic granules.[11]

One milliliter of blood was inoculated aseptically into 20ml of brain heart infusion broth for culture and sensitivity. Newborn infants with positive blood cultures were considered to have proven sepsis while the others were still considered as clinically suspected of infection.

The clinical manifestations and hematological parameters were compared, individually and in combination, with the blood culture result.

Statistical analysis

Data were analyzed by using T-test to compare two groups with numerical data, Chi-square test to compare or associate nominal data and Fisher Exact test when the expected frequencies are less than 5. A level of 0.05 was considered statistically significant. The reference values of the neonatal hematological parameters of Manroe, et al were used as the standard values.[12] The maternal reference values used were taken from the values for pregnancy.[13-14] The results that were statistically significant in this study were used to design a hematologic scoring system that will predict the probability of sepsis.

RESULTS

Neonatal profile and neonatal sepsis

There were 17 neonates who had culture proven sepsis which had a prevalence of 17%. Eleven of the 17 neonates were preterm (64.7%) and 6 were full term neonates (35.3%). There was a significant correlation between preterm and positive blood culture with p value of 0.047. The neonatal profile showed that 12 males (70.6%), 11 appropriate for gestational age (64.7%) with mean birth weight of 2000 grams and 11 infants delivered via caesarian section (64.7%) had culture proven sepsis. However, these data were not significant (Table 1).

Table 1: Association of neonatal profile with neonatal sepsis

Patient's Profile	Blood CS (+) (n=17)	Blood CS (-) (n=83)	Total	*p* value
Pre-term	11 (64.7%)	32 (38.6%)	43	0.047 (S)
Full-term	6 (35.3%)	51 (61.4%)	57	(chi-square test)
Sex				
Male	12 (70.6%)	50 (60.2%)	62	> 0.05 (NS)
Female	5 (29.4%)	33 (39.8%)	38	(chi-square test)
Weight(gm)				
Mean +/- SD	2012+/-920.7	2289+/-768.6		> 0.05 (NS)
Range	1000 – 3800	1000 – 3900		(t-test)
Weight for pediatric age				
AGA	11 (64.7%)	63 (75.9%)	74	> 0.05 (NS)
LGA	2 (11.8%)	1 (1.2%)	3	> 0.05 (NS)
SGA	4 (23.5%)	19 (22.9%)	23	> 0.05 (NS) (Fisher test)
Manner of Delivery				
LSCS	11 (64.7%)	41 (49.4%)	52	
OFE	0 (0%)	7 (8.4%)	7	> 0.05 (NS)
SVD	6 (35.3%)	35 (42.2%)	41	(chi-square test)

The bacterial species isolated showed that 14 of the 17 (82.3%) blood culture isolates were Alkaligenes faecalis followed by Acinetobacter (n=1), Diphteroides (n=1) and Staphylococcus epidermidis (n=1).

Clinical profile and neonatal sepsis

Majority of the clinical manifestations of the newborns who were suspected with sepsis had concomitant respiratory diseases (n=77) and only 23 patients had primary impression of sepsis clinically or based on the maternal history of infection. Among the neonates with culture proven sepsis, there were 12 neonates who had respiratory problems (70.6%).

There were 13 out of the 67 mothers who had illnesses during pregnancy with culture proven sepsis as shown in Table 2. The maternal illnesses were upper respiratory tract infection, urinary tract infection, and premature rupture of membrane.

It was also noted that there were no significant difference in the Apgar scores, neonatal symptoms and maternal illnesses.

Table 2: Association of the neonatal clinical symptoms and maternal symptoms with Neonatal Sepsis

Clinical profile	Blood CS (+) (n=17)	Blood CS (-) (n=83)	Total	p value
Apgar score at 1-min 1 – 3 4 – 6 7 – 9 Mean	 4 (23.5%) 4 (23.5%) 9 (52.9%) 6	 14 (16.9%) 18 (21.7%) 51 (61.4%)%6 1 (1.2%)	 18 22 60	 > 0.05 (NS)
Apgar score at 5-mins 3 4 – 6 7 – 9 10 Mean	 1 (5.9%) 4 (23.5%) 12 (70.6%) 0 8	 9 (10.8%) 71 (85.5%) 2 (2.4%) 8 18	 2 13 83 2	 > 0.05 (NS)
Neonatal Symptoms Rule out Sepsis HMD TTN Pneumonia MAS	 5 (29.4%) 6 (35.3%) 1 (5.9%) 3 (17.6%) 2 (11.8%)	 (21.7%)14 (16.9%)20 (24.1%)17 (20.4%)14 (16.9%)	 23 20 21 20 16	 > 0.05 (NS) (chi-square test)
Maternal Symptoms (+) (-)	 13 (76.5%) 4 (23.5%)	 54 (65.0%)29 (35.0%)	 67 33	 > 0.05 (NS) (chi-square test)

Neonatal hematological parameters and neonatal sepsis

The details of the neonatal hematological parameters are shown in Table 3. The mean total leukocyte count of the neonates with sepsis was significantly lower than those without sepsis (p=0.03). However, when compared to the reference values, there was no significant difference. It could be noted that there were 14 neonates with sepsis (82.4%) whose total leukocyte count were within the normal range. The nucleated red blood cells, total neutrophil count or segmenters, lymphocytes, immature cells, I/T ratio, I/M ratio, absolute neutrophil count and toxic granules were not statistically significant. It was only the platelet count which was significant (p=0.02) when compared to the reference value.

Table 3: Association of the Neonatal Hematological Parameters with Neonatal Sepsis

Hematological parameters	Blood CS (+) (n=17)	Blood CS (-) (n=83)	Total	p value
NRBC Mean +/- SD Range Median	 25.24 +/ - 44.81 0 – 146 2	 5.46 +/ - 13.54 0 – 85 2	 	 0.05 (NS) (t-test)
NRBC 0 >0	 7(41.2%) 10 (58.8%)	 39 (47.0%) 44 (53.0%)	 46 54	 >0.05 (NS) (chi-square
TLC (x10^9/L) Mean +/- SD Range Median	 12.14 +/- 8.68 4.50-41.90 10.2	 16.66 +/ -7.78 1.70 – 41.00 15.6	 	 0.03 (S)
TLC (x10^9/L) ≤ 5 or ≥25 Normal	 3 (17.6%) 4.50-41.90 14(82.4%)	 13 (15.7%) 70 (8 4.03 15.6	 16 84	 >0.05 (NS) (Fisher test)
TLC (x10^9/L) Mean +/- SD Range Median	 6.29 +/- 7.54 1.02-32.85 3.50	 9.17 +/ -6.34 0.48-28.56 8.10	 	 0.05 (NS) (t-test)
TNC(x10^9/L) <0.78 or 1.45 Normal	16 (94.1%) 1 (5.9%)	81 (97.6%) 2 (2.4%)	97 3	>0.05 (NS) (Fisher test)
Lymphocytes (x10^9/L) Mean+/-SD Range Median	 4.17+/-2.75 1.08-12.32 4.04	 5.60+/-3.17 0.18-16.71 4.85	 	 0.05 (NS) (test)
Immature Mean +/- SD Range Median	 0.64 +/ - 1.26 0 – 4.45 0	 0.52 +/ - 1.22 0 – 6.97 0	 	 > 0.05 (NS) (t-test)
Immature<0.05 or >1.45 Normal	 16 (94.1%) 1 (5.9%)	 73 (88%) 10 (12%)	 89 11	 > 0.05 (NS) (Fisher test)

Table 3: Association of the Neonatal Hematological Parameters with Neonatal Sepsis (cont'd)

Hematological parameters	Blood CS (+) (n=17)	Blood CS (-) (n=83)	Total	p value
I/T Mean +/- SD Range Median	0.108 +/ - 0.197 0 – 0.640 0	0.063 +/ -0.131 0 –0.784 2		0.05 (NS) (t-test)
I/T >0.16 ≤0.16 square	4(23.5%) 10 (58.8%)	13 (15.7%) 44 (53.0%)	17 83	>0.05 (NS) (Fisher-test)
I/M Mean +/- SD Range Median	0.216+/ -0.473 0-1.790 0	0.074 +/ -0.159 0 – 0.750 0		0.05 (NS) (t-test)
I/M > 0.3 ≤ 0.3	3 (17.6%) 14 (82.4%)	7 (8.4%) 76 (91.6%)	10 90	>0.05 (NS) (Fisher test)
ANC Mean +/- SD Range Median	7164 +/ -7291 1620-32500 5044	9788 +/ -6745 582 -34850 8959		0.05 (NS) (t-test)
Platelet count (x10⁹/L) Mean+/-SD Range Median	200.5+/ -108.8 54-375 203.50	243.4 +/ -85.4 55-456 243.00		0.05 (NS) (test)
Platelet count (x10⁹/L) Mean+/-SD ≤ 150 > 150	6 (35.3%) 6 (35.3%) 11 (64.7%)	9 (10.8%) 55-456 74 (89.2%)	15 85	0.02 (S) (Fisher test)
Toxic granules (+) (-)	6(35.3% 11 (64.7%)	30 (36.1%) 53 (63.9%)	36 64	>0.05 (NS) (chi-square test)
Toxic granules ≥ 3 + < 3 Normal	0 (0%) 17 (100%)	0 (0%) 83 (100%)	0 100	NA

Maternal hematological parameters and neonatal sepsis

The obtained results of the maternal total leukocyte count showed no significant difference but when compared to the reference value for pregnant women[12], the results were significant. There were 94.1% mothers who had leukocytosis in the confirmed sepsis group with p value of 0.006. The other hematological parameters namely segmenter, lymphocyte and platelet count had no statistical significance (Table 4).

Table 4: Association of the Maternal Hematological parameters with Neonatal Sepsis

Maternal parameters	Blood CS(+) (n=17)	Blood CS(-) (n=83)	Total	*p*-value
WBC (x10⁹/L) Mean +/- SD Range Median	15.47+/-3.61 9.3–23.19 15.30	14.29 +/- 5.18 5.9 – 30.4 13.20		> 0.05 (NS) (t-test)
WBC (x10⁹/L) >12 ≤12	16 (94.1%) 1(5.9%)	49 (59.0%) 34 (41.0%)	65 35	0.006 (S) (chi-square test)
Segmenter (x10⁹/L) Mean +/- SD Range Median	12.53+/- 3.89 6.70–21.24 12.71	11.01 +/-4.76 7.87 – 25.84 10.19		> 0.05 (NS) (t-test)
Segmenter (x10⁹/L) 1.8 – 7 <1.8 – >7	1 (5.9%) 16 (94.1%)	1 (1.2%) 82 (98.8%)	2 98	> 0.05 (NS) (Fisher-test)
Lymphocyte (x10⁹/L) Mean +/- SD Range Median	1.85 +/- 0.9 0.88–3.84 1.71	2.18 +/- 1.13 2.33 – 7.44 1.97		> 0.05 (NS) (t-test)
Lymphocyte (x10⁹/L) 1 – 4.8 < 1 - > 4.8	16 (94.1%) 1 (5.9%)	75 (90.4%) 8 (9.6%)		> 0.05 (NS) (Fisher-test)
Platelet count (x10⁹/L) Mean +/- SD Range Median	335.7+/- 97.3 135 – 467 336	292.5 +/- 101.5 69 – 677 277		> 0.05 (NS) (t-test)
Platelet count (x10⁹/L) 150 - 400 < 150 - > 400	0 (0%) 17 (100%)	1 (1.2%) 82 (98.8%)	1 99	> 0.05 (NS) (Fisher-test)

Correlation of neonatal and maternal factors with neonatl sepsis

The factors which showed statistical significance were preterm neonates, neonatal platelet count and maternal total leukocyte count. In table 5, the odds ratio of having a positive blood culture result was 3 times (OR = 2.92) higher for preterm as compared to full term neonates. The odds ratio for neonates with low platelet count was 5 times (OR = 4.74) higher than the neonates whose platelet count was within normal range. Lastly, for neonates whose maternal total leukocyte count (TLC) was >12, the odds ratio was 11 times higher for neonatal sepsis as compared to patients whose maternal TLC was ≤12. Among these factors, the maternal total leukocyte count had the highest sensitivity of 94.1% and negative predictive values of 97.1% (Table 6).

Table 5: Factors Associated with Neonatal Sepsis

Factors	OR	95% CI	p value
Preterm	2.92	0.88 – 9.98	< 0.05
Neonatal Platelet count (≤150)	4.74	1.16 – 19.65	< 0.05
Maternal TLC (>12)	11.1	1.42 – 87.73	< 0.01

Table 6: Sensitivity, Specificity of Factors Associated with Neonatal Sepsis

Factors	Sensitivity	Specificity	PPV	NPV
Preterm	64.7	60.2	25.0	89.3
Neonatal Platelet count (≤150)	35.3	89.2	40.0	87.1
Maternal TLC (>12)	94.1	41.0	24.6	97.1

A scoring system was devised based on the significant factors that were obtained in this study. There is a significant difference in the median scores of the patients with positive blood culture and negative blood culture. Higher median scores were noted among the neonates with positive blood culture (Table 7).

Table 7: Scoring

Scores	Bld CS (+)(n=17)	Bld CS (-)(n=83)	Total
0	0 (0%)	21 (100%)	21
1	5 (11%)	39 (89%)	44
2	9 (30%)	21 (70%)	30
3	3 (60%)	2 (40%)	5

p <0.001 (S)

Since the median scores were significantly different, each score was then computed for its individual accuracy of determining sepsis. A score of 3 was both highly sensitive and specific for neonatal sepsis. The chance of getting a positive blood culture given all the 3 factors was 100%. While, if the factor were absent, the chance of a negative blood culture was 91.3% (Table 8).

Table 8: Sensitivity, Specificity of Score Associated with Neonatal Sepsis

Scores	Sensitivity	Specificity	PPV	NPV
1	100	35.0	11.4	100
2	100	50.0	30.0	100
3	100	91.3	60.0	100

DISCUSSION

A high index of suspicion is important in the diagnosis and treatment of neonatal infection because it is hampered by vague, nonspecific or nonexistent clinical manifestation. Thus, it is difficult to establish a diagnosis based on clinical picture alone. However, it is imperative that treatment is instituted early because of the high mortality associated with the neonatal infection.

In this study, there was 17% culture proven neonates with sepsis which were predominantly preterm (64.7%) and males (70.6%). This was possibly due to impaired defense mechanisms and low immunoglobulin G levels in males and low birth weight neonates.[15] In addition, newborns particularly the preterm, have less effective phagocytosis and chemotactic activity. Therefore, rapid invasion of offending organism occur very fast. They also have relative immunoglobulin M deficiency rendering them more vulnerable to gram negative infections.[16]

Infections occurring at less than 72 hours of age usually are caused by bacteria acquired in utero or during delivery, whereas infection after that time most likely have been acquired after birth.[13] Thus, it is essential to know the maternal illnesses which can predispose to neonatal sepsis. These are prolonged rupture of membranes, foul smelling amniotic fluid, maternal fever or other symptoms suggestive of infection, unexplained fetal distress and previous septic infant. It was noted that there were 76.5% neonates with culture proven sepsis who had maternal history of infection. However, the result showed no significant difference which could be attributed to prior antibiotic intake of the mothers during the time of illness.

The most common presenting symptom in the early onset of sepsis is respiratory distress. It is

manifested most commonly on the first day of life, with majority of cases at less than 12 hours.[6] This was evident in this study wherein there were 77 out of the 100 neonates (77%) presented with respiratory problems. Other clinical signs of bacteremia include unexplained low Apgar scores, poor perfusion, hypotension, bradycardia, and unstable temperature.

Because of the low positivity of blood culture, its inavailability in some peripheral health centers and the time allotted for the result to be obtained, the need for other tests in diagnosing neonatal septicemia is warranted.[1]

The complete blood count with differential is widely used, either singly or in conjunction with other test or clinical findings, as a diagnostic tool for neonatal sepsis. [17]

The criteria of Manroe with 2 of 3 indices (total PMN count, immature PMN count, and I/T ratio) abnormal were the most reliable of the published criteria evaluated and would have identified all infants with sepsis and all infants with probable sepsis.[12,17]

In this study, there were more hematological parameters of the neonates studied. These were total leukocyte count, total neutrophil count, immature cells, immature to total neutrophil cells (I/T) ratio, immature to mature cells (I/M) ratio, platelet count and toxic granulation. Nucleated red blood cells, lymphocytes and absolute neutrophil count were also included because there were no studies done yet in determining its association with sepsis. Moreover, maternal infection was noted to be one of the major risk factors in early neonatal sepsis which could be documented by a complete blood count. Thus, the maternal hematological parameters, consisting of total leukocyte count, total neutrophilic count, lymphocytes and platelet count, were also used as indices in predicting neonatal sepsis.
In the neonatal hematological parameter, only the platelet count was significant with p value of 0.02.

Thrombocytopenia was seen frequently in sepsis proven group. This could result from increased platelet destruction, sequestration secondary to infections, failure in platelet production due to decreased number of megarkaryocytes or damaging effects of endotoxin on the platelets.[11]

Total leukocyte count, total neutrophilic count and immature cells showed no significant association with sepsis. In a study by Akenzua, it was stated that total neutrophil count was of limited value for the diagnosis of infection since elevation is often late and inconsistent. In addition, newborn infants with proven bacterial infection had normal neutrophil count but the bands increased beyond the normal range.[18] In another study, although neutropenia in the newborn is most often secondary to infection, there are many causes of neutropenia including isoimmune neutropenia, congenital neutropenia, and neutropenia due to inborn error of metabolism.[19] Lastly, neutrophilia in the absence of an increase in band may occur in patients with no evidence of infection, presumably the result stress or other non specific causes. Therefore, neutrophilia itself is not a reliable or sensitive test of infection.[11]

Neutrophil ratios were often abnormal during neonatal sepsis. However, this was not evident in this study possibly because of the variation in interpretation of peripheral smears by different observers.

Toxic granules also showed no significant difference in this study. The presence of toxic granules represents the production of unusual neutrophils during the stress leucopoiesis and infection. It is invariably present during sepsis, a change never seen in healthy newborn infants but are not always increased in infection. [11] The other parameters, namely: nucleated red blood cells, lymphocytes and absolute neutrophilic count, were not statistically significant.

The maternal hematological parameter which showed significant correlation between sepsis was total leukocyte count with a negative predictive value of 97.1%. The leukocyte count usually ranges from 5,000 to 12,000 x 10^9/L. During labor and the early puerperium, it may be markedly elevated. The cause is not known but probably represents the reappearance in the circulation of leukocytes previously shunted out of the active circulation. During pregnancy, there is neutrophilia that consists of mature forms.[13]

In this study, there were 3 parameters, namely: preterm neonates, neonatal platelet count of $\leq$150 x 10^9/L, and maternal total leukocyte count of > 12,000 x 10^9/L that were statistically significant. Based on these factors, a scoring system was formulated which could be used in determining the presence of sepsis. The presence of one factor corresponded to a score of 1 which indicated a positive predictive value of 11% and a score of 2 indicated 30% positive predictive value. The probability of getting a positive blood culture increases with an increasing score. The highest score was 3 with 100% sensitivity and 91.3% specificity for predicting neonatal sepsis.

It could be noted that in this study, there were different parameters used for predicting sepsis compared to other hematological scoring sytem.[12] This was because

the said parameters were the ones found to be statistically significant. The difference in the sensitivity of hematological values to other studies could be due to wide range of the subjects and some degree of observer variability in reporting the peripheral smear.

CONCLUSION

Neonatal sepsis, especially in its early stages, may be difficult to diagnose because of its nonspecific clinical symptoms. Because the prognosis for sepsis largely depends on early identification and treatment, these neonates are subjected to extensive diagnostic evaluation and empiric treatment.

The usefulness of a scoring system based on the clinical manifestations of the neonate and mother supported by their hematological parameters can provide information in determining the probability of sepsis in neonates. Since this scoring system is highly sensitive and specific for neonatal sepsis, it could also serve as the basis for a more rational approach to antibiotic use. A significant decrease in the use of antibiotics may prevent the emergence of resistant organisms, decrease the chance of side effects and minimize cost.

RECOMMENDATIONS

It is recommended that more subjects will be included in future studies wherein there will be a control group composed of healthy, asymptomatic neonates and a test group composed of neonates with probable sepsis or proven sepsis. The group can also be divided into full term or preterm neonates to determine differences in their hematological characteristics. It also suggested that one interpreter of the laboratory results be assigned to decrease the observer variability.

REFERENCES

1. Manucha V, Rusia U, Sikka M, Faridi MMA, Madan N. Utility of hematological parameters and C-reactive protein in the detection of neonatal sepsis. Journal of Pediatrics and Child Health. 2002; 38: 459-464.
2. Baley J, Goldfarb J, Neonatal Infections. Care of the high risk neonate, 4th edition. MH. MH Klaus and AA Fanaroff: editors. Philadelphia: WB Saunders Company, 1993.
3. David E., Tan CT, Que SP., Cruz NGS. Determining the criteris for early discontinuation of antibiotic therapy in suspected neonatal sepsis. Philippine Journal of Microbial Infectious Diseases. 1980; 9 (2): 145-155.
4. Annual Reports of the Section of Neonatology of the Department of Pediatrics UP-PGH Medical Center. 2000-2002.
5. Bellig L, Ohning B. Neonatal Sepsis. EMedicine Journal Pediatrics/Neonatology. 2003; 4(1). 6. Thilo EH, Rosenberg AA. Infections of the Newborn. Current Pediatric Diagnosis and Treatment, 14th edition. Hay WW, Hayward AR, Levin MJ, Sondheimer JM: editors. New Jersey: Appleton and Lange, 1999.
7. Fowlie PW, Schimdt B. Diagnostic tests for bacterial infection from birth to 90 days- a systematic review. Archives of the Diseases in Child Fetal Neonatal Edition. 1998; 79: 92-98.
8. Kite P, Millar MR, Gorham P, Congdon P. Comparison of five tests used in diagnosis of neonatal bacteremia. Archives of Disease in Childhood. 1988, 63: 639-643.
9. Da Silva O, Ahisson A, Kenyon C. Accuracy of leukocyte indices and C-reactive protein for the diagnosis of neonatal sepsis: a critical review. Pediatric Infectious Diseases Journal. 1995; 14: 362-366.
10. Philip AG. Decreased use of antibiotics using a neonatal sepsis screening technique. The Journal of Pediatrics. 1981, 98(5): 795-799.
11. Zipursky A, Palko RT, Milner MIS, and Akenzua MB. The Hematology of Bacterial Infections in Premature Infants. Pediatrics. 1976, 57(6): 839-853.
12. Manroe BL, Weinberg AG, Rosenfeld CR, Browne R. The neonatal blood count in health and disease. The Journal of Pediatrics. 1979, 95(1): 89-98.
13. Cunningham FG, Grant N. Maternal Adaptations to Pregnancy. Williams Obstetrics, 21st edition. New York: Mc Graw Hill Medical Publishing Division. 2001.
14. Nelson DA, Morris MW. Basic Examination of Blood. Clinical Diagnosis and Management, 18th edition. Henry JB: editors Philadelphia: W.B. Saunders Company. 1991.
15. Anwer S, Mustafa S. Rapid Identification of Neonatal Sepsis. Journal of Pakistan Medical Association. 2000; 50(3).
16. Limjoco-Sarte L, Gonzales RM. Septicemia in Filipino Infants and Children: Analysis of 724 Bacteriologicallly Proven Cases in an Urban Hospital. Philippine Journal of Pediatrics. 1981; 30(6): 190-198.
17. Rodwell RL, Tudehope DA. Early diagnosis of neonatal sepsis using a hematologic scoring sytem. The Journal of Pediatrics. 1988; 112(5): 761-767.
18. Akenzua GI, Hui YT, Milner R, Zipursky A. Neutrophil and Band counts in the Diagnosis of Neonatal Infections. Pediatrics. 1974; 54(1): 38-42.
19. Engle WD, Rosenfeld CR. Neutropenia in high risk neonates. The Journal of Pediatrics. 1984; 105(6): 982-986.