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Factors associated with mortality outcomes in neonatal septicemia in a tertiary care unit

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Abstract

Background: Neonatal Septicemia is a major cause of mortality and morbidity in newborns both in developed and developing countries.

Objective: The objective of this study was to determine the risk factors for mortality in neonatal septicemia. **Materials and Methods:** This retrospective case-control study was conducted in Srinagarind Hospital, Khon Kaen, Thailand. The study considered the demographics, laboratory results, and clinical features for a total of 133 patients during the period May 2005- September 2010. Thirty four out of these patients died from their condition.

Results: Investigation of neonatal demographics found that low Apgar scores in 1 minute (OR 12.237, P<0.001) and 5 min (OR 13.143, P <0.001), VLBW (OR 5.312, P 0.001) , EOS (3.749, P 0.001), prematurity (2.723, P 0.01), and

out born delivery (6.253, P<0.001), were all significantly associated with fatality. Laboratory results showed that hyperglycemia (OR 6.213, P 0.001) and thrombocytopenia (3.853, P 0.002), were significant contributors to fatality. Among all clinical features, lethargy (14.667, P <0.001), apnea (OR 13.160, P<0.001), poor feeding (OR 7.807,P<0.001), hypothermia (OR 4.807, P <0.001) and jaundice (OR4.769< P0.007), were significantly associated with fatality. Gram-negative bacteria were frequently isolated from dead septicemic neonates. E. coli was the most common bacteria isolated from dead septicemic neonates (18.2%), followed by Klebsiella spp. (15.9%), Enterobacter spp. (15.9%), Acinetobacter spp. (13.6%) and Pseudomonas spp. (11.3%).

Conclusion: Early detection and management of these associated factors are necessary to

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prevent severe and life threatening complications and death in neonatal septicemia. Strict infection control measures remain the mainstay in the management of the multidrug resistant bacterial infections in neonates

1. INTRODUCTION

Over 130 million babies are born every year. Four million newborns, worldwide die within their 28 days of life, and over 3 million newborns die in first week after birth [1]. Neonatal Septicemia is a major cause of mortality and morbidity in newborns both in developed and developing countries [2]. It is responsible for 30-50% of total neonatal death in developing countries [3]. Despite advances in neonatal care, overall case fatality rates from septicemia range from 2% to as high as 50% [4]. Infection cause 1.6 million infants death in developing countries each year [1]. Up to 50% of neonatal intensive care unit (NICU) patients experience one or more episodes of septicemia, which is associated with an increased risk of long term sequelae [5].

The frequency of death is significantly higher in preterm babies. Low birth weight, IUGR,. Also highest mortality is associated with blood culture positive for gram negative bacteria and Staphylococcus aureus [6].

2. MATERIALS AND METHODS

Study design: This was a retrospective case control study. Data were compiled from microbiology laboratory and medical record. The study was conducted from October 2010 to March 2011 in Srinagarind Hospital, Faculty of Medicine, Khon Kaen University, located in Khon Kaen province in northeast Thailand.

Data source: Microbiology data and Medical record of neonatal patients in Srinagarind Hospital from May 2005 to September 2010

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Inclusion criteria

1. Age equal or less than 28 days at the onset of illness.
2. The blood culture is positive for bacteria.
3. The medical records are available.

Exclusion criteria

1. The culture result is positive only for fungus.

The medical record is not available. Sample size calculation: Sample size calculation: Sample size calculation was performed using Epi info 6 version 3.5.1. The estimated sample sizes are 34 for case and 99 for control group. The ratio of case and control from is 1:3. Total estimated study group of neonatal septicemia are 133 neonates. and percentage for categorical variables. The differences in clinical features and laboratory findings of neonatal septicemia between fatal and survival outcome were compared using odds ratio and Chi-square test or Fischer-exact test for categorical variables and student's t-test or Mann Whitney U test or one way ANOVA test for continuous variable as appropriate. SPSS 15 statistical software was used for all calculations.

P-value of less than 0.05 was considered statistically significant, P-value <0.01 as highly significant and P-value <0.001 was extremely significant.

Study procedure: Data collection: The list of the neonatal septicemia patients with positive hemoculture were retrieved from microbiological records in laboratory. The patient's medical records were then collected from hospital registry, and then check for the inclusion criteria. The medical records from eligible patients were reviewed, and information was transferred to the case record form. The neonatal septicemia patients with positive blood culture who died were assigned as the case group, whereas the neonatal septicemia patients with positive blood culture who survived were the control group.

Data Management: After all raw data were transferred; data cleaning process was done. Illogical numbers (no data, negative number and blank item) were rechecked. The original medical record was explored again if necessary. Then some variables were added based on the raw data. **Ethical committee approval:** Ethical approval of this study was obtained from 2 ethical committees, the Faculty of Tropical Medicine, Mahidol University, and Faculty of Medicine Khon Kaen University, both in November 2010.

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3. RESULT

Medical records searching

During the study, 285 neonates with positive blood culture from May 2005 to September 2010 were found from microbiology laboratory data, among them 50 were died and 235 were survived. In dead neonates 34 met the inclusion criteria and included in the study. Sixteen were excluded From 235 survived patients, 99 were selected randomly. The diagram of the medical records Regarding patients demographic data, early onset septicemia [19 (55.9%)] (Odds Ratio 3.749, P 0.001), very low birth weight (VLBW)[17 (50.0)] (OR 5.312, P0.001), preterm delivery [23 (67.7%)] (OR 2.723, P0.01), Out born neonates [24 (70.9%)] (OR 6.253, P <0.001) low Apgar score (0-3) at first minute [15, (44.1%)] (OR
12.237, P<0.001) and 5 minute (≤6) [17 (50.0%)],
(OR 13.143, P<0.001), has significant association with fatality. The demographic data has shown in table 1.

Table 1: Demographic risk factors for fatality in neonatal septicemia

Variable	Dead (N=34) n.%	Alive (N=99) n. %	OR	95% CI Lower - Upper	P value
EOS	19 (55.9)	25 (25.2)	3.749	1.660-8.468	**0.001**
LOS	15 (44.1)	74 (74.8)			
VLBW (<1500gm)	17 (50.0)	22 (22.2)	5.312	2.004-14.084	**0.001**
Preterm (<37wk GA)	23 (67.7)	43 (43.4)	2.723	1.189-6.189	**0.01**
Site of delivery					
• Srinagarind Hospital	9 (26.9)	68 (68.7)			
• Out born	24 (70.6)	29 (29.3)	6.253	2.592-15.091	**<0.001**
Apgar score 1 min					
• 0-3	15 (44.1)	6 (6.1)	12.237	4.207-35.593	**<0.001**
• 4-10	19 (55.9)	93 (93.9)			
Apgar score 5 min					
• =6	17 (50.0)	7 (7.1)	13.143	4.734-36.485	**<0.001**
• >6	17 (50.0)	92 (92.9)			

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Regarding the neonates clinical data, Lethargy [22 (64.7%)] (OR 14.667, P <0.001),Apnea [14 (41.2%) (OR 13.160 P<0.001),Poor feeding [15 (44.1%)] (OR 7.807, P<0.001), Hypothermia [23 (67.7%)] (4.807, P <0.001), and Jaundice [7 (20.6%)] (OR4.769, P 0.007), has significantly association with mortality outcome table 2.

Table 2: Clinical risk factors for fatality in neonatal septicemia

Variable	Dead (N=34) n. %	Alive (N=99) n %	OR	95% CI Lower-Upper	P value
Lethargy					
• Yes	22 (64.7)	11 (11.1)	14.667	5.717-37.626	**<0.001**
• No	12 (35.3)	88 (88.9)			
Apnea					
• Yes	14 (41.2)	5 (5.1)	13.160	4.254-40.716	**<0.001**
• No	20 (59.8)	94 (94.9)			
Poor feeding					
• Yes	15 (44.1)	9 (9.1)	7.807	2.972-20.460	**<0.001**
• No	19 (55.9)	89 (89.9)			
Hypothermia					
• Yes	23 (67.7)	30 (30.3)	4.807	2.083-11.102	**<0.001**
• No	11 (32.3)	69 (69.7)			
Jaundice					
• Yes	7 (20.6)	6 (6.1)	4.769	1.519-14.977	**0.007**
• No	27 (79.4)	93 (93.9)			

The results of blood glucose and platelet counts are presented in table 3.In our study, Hyperglycemia [11 (32.4%)](OR 6.213, P 0.001) and Thrombocytopenia [18 (52.9%)] (OR 3.853, P 0.002) have association with fatality in neonatal septicemia.

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Variable	Dead (N=34) n. %	Alive (99) n. %	OR	95% CI Lower-Upper	P value
Hyperglycemia	11 (32.4)	6 (6.1)	6.213	2.017-19.139	**0.001**
Thrombocytopenia	18 (52.9)	23 (23.2)	3.853	1.660-8.961	**0.002**

Regarding causative organisms, it was found that gram negative bacteria were isolated more frequently from death neonates. In this study *E.coli*was the commonest bacteria isolated from dead neonates (18%) followed by *klebsella* spp (15.9%), *enterobacter* spp (15.9%), *acinetobacter* spp (13.6%) and *pseudomonas* spp(11.3%). Gram positive bacteria were frequently isolated from survive neonates compare to dead septicemic neonates.

Organism	Dead n. %	Alive n. %
Gram negative		
• *Escherichia coli*	8(18.2)	3 (3.0)
• *Klebsiella* spp.	7 (15.9)	11 (11.1)
• *Enterobacter* spp.	7(15,9)	1 (1.0)
• *Acinetobacter* spp	6 (13.6)	7 (7.1)
• *Pseudomonas* spp.	5 (11.3)	3 (3.0)
• *Citrobacter freundi*	0 (0.0)	1 (1.0)
Gram positive		
• *Staphylococcus aureus*	3 (6.8)	14 (14.1)
• *Enterococci* spp.	3 (6.8)	21 (21.2)
• Coagolase negative *Staphylococcus*	2 (4.5)	18 (18.2)
• Group B *streptococci*	2 (4.5)	9 (9.1)
• *Streptococcus virdan*	1 (2.7)	11 (11.2)
Total	**44**	**99**

4. DISCUSSION

Neonatal Septicemia is a major cause of mortality and morbidity in newborns both in

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developed and developing countries [2]. It is responsible for 30- 50% of total neonatal death in developing countries [3]. We have used a case control approach to identify the risk factors for mortality outcome in neonatal septicemia.

As shown in this study, the number of EOS was higher in dead patients so, it was the significant risk factor for mortality. The same result was reported from many countries[6, 7]. the frequency of VLBW (<1500gm) was higher in dead (50.0%) compared to survived neonates (22.2%), it was the potential risk factor for neonatal death. As well as the frequency of preterm delivery (<37 weeks gestation) was also higher in dead compared to survived neonates. It was a significant risk factor among dead neonates. Premature and low birth weight infants are at increased risk for developing complications of septicemia because of deficiencies in humoral and cellular immunity [8, 9]. Similar were the observations of different workers, who reported significant risk in prematurity and low birth weight[6, 10]. In this study, when we compared Apgar score at 1 min between two groups, there were statistically higher proportion of low Apgar score (0-3) in dead neonates than survived patients. Similarly, when comparing Apgar score at 5 minutes, dead neonates more frequently had Apgar score of ≤6.A study from Denmark reported the same results[11]. In this study among the clinical signs and symptoms, apnea, lethargy, and poor feeding, jaundice were statistically significant associated with dead in neonatal septicemia patients. The same result was reported from Tanzania [12].Regarding laboratory parameters, thrombocy- topenia had statistically significant association with mortality outcome in this study. Most of the studies documented the association of thrombocytopenia with gram negative bacterial septicemia[13, 14].A study from Iran reported the association of thrombocytopenia and mortality from neonatal septicemia [15]. Hyperglycemia is a risk facto In this study we have found the statistically significant association between hyperglycemia and neonatal mortality from neonatal septicemia. A study from Netherland similarly has found the association of hyperglycemia and mortality from neonatal septicemia and other comorbidities[16]. A study from United States reported the relation of hyperglycemia and mortality from septicemia in low birth weight neonates [17].In this study, It was found that gram negative bacteria were isolated more frequently from dead neonates

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than from survived neonates. Many study reported the same result[6, 12].In this study among gram negative microorganisms, *E.coli* was the commonest bacteria isolated from dead neonates (18%) followed by *klebsella* spp (15.9%), *enterobacter* spp (15.9%), *acinetobacter* spp (13.6%) and *pseudomonas* spp(11.3%). The same result was observed in a study from Tanzania, which reported high mortality rate with *E. coli* neonatal septicemia followed by *Klebsiella* spp [18].

5. CONCLUSION

Neonatal septicemia is a major cause of morbidity and mortality among children in both developed and developing countries.

Investigation of neonatal demographics found that low Apgar scores in 1 minute and 5 min, VLBW, EOS, prematurity, and out born delivery, were all significantly associated with fatality. Laboratory results showed that hyperglycemia and thrombocytopenia, were significant contributors to fatality. Among all clinical features, lethargy, apnea, poor feeding, hypothermia, and jaundice were significantly associated with fatality. Gram-negative bacteria were frequently isolated from dead septicemic neonates. *E. coli* was the most common bacteria isolated from dead septicemic neonates, followed by *Klebsiella* spp., *Enterobacte*r spp., *Acinetobacter* spp., and *Pseudomonas* spp.

Early detection and management of these associated factors are necessary to prevent severe and life threatening complications and death in neonatal septicemia. Strict infection control measures remain the mainstay in the management of the multidrug resistant bacterial infections in neonates.

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