

RISK FACTORS FOR NEONATAL *KLEBSIELLA* SEPTICEMIA IN SRINAGARIND HOSPITAL

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Abstract. Three years' data were analysed to assess the risk factors for neonatal *Klebsiella* septicemia in Srinagarind Hospital. The incidence of *Klebsiella* septicemia was 4.1 per 1,000 livebirths or 5.2 per 100 discharged infants. Eighty-two per cent of infected cases were low birth weight infants and 67.7% were born prematurely. From multivariate analysis, the risk factors were endotracheal intubation (OR 31.57, 95% CI 289-343.82) and central venous catheterization (OR 16.99, 95% CI 1.15-250.37). The overall mortality rate was 67.7%.

Periodic review and continuous reinforcement of infection control policies in the neonatal unit are of paramount importance to decrease the incidence of nosocomial infection and successful control of outbreaks as well.

INTRODUCTION

Neonatal septicemia has been recognized as a major problem in the neonatal intensive care unit. During the past decade, infection by gram negative bacilli such as *E. coli* and *Klebsiella* species has been a problem. More recently, although staphylococcal infection has become the most important problem in modern intensive care units in developed countries (Donowitz *et al*, 1987; Sidebottom *et al*, 1988; Freeman *et al*, 1990), gram negative bacilli still remain the common pathogens in the high risk neonatal intensive care unit, especially in developing countries. Most of the reported outbreaks of gram negative bacilli infections were due to *Klebsiella* species (Hable *et al*, 1972; Mayhall *et al* 1980; McKee *et al*, 1982; Saravolatz *et al*, 1984), and a majority of the infants had gastrointestinal (GI) colonization. A common source is usually not found and colonized infants serve as reservoirs during such outbreaks.

In the neonatal unit of Srinagarind Hospital, we encountered several outbreaks of *Klebsiella* septicemia during the 3-year period from 1987 to 1989.

A crowded intensive care environment, a shortage of nursing staff and invasive procedures seemed to influence the infection rate. We therefore carried out this study to determine the risk factors for neonatal *Klebsiella* septicemia.

MATERIALS AND METHODS

A retrospective case controlled study was done to identify the risk factors for *Klebsiella* septicemia. Hospital records of the patients who were admitted to the neonatal unit from January 1, 1987 to December 31, 1989 were analysed.

A case was defined as an infant from whom *Klebsiella* was isolated from blood with signs and symptoms of systemic illness. One control for each septicemic case was non infectious patient and was selected from those who were admitted during the 14-day period immediately preceding the bacteremic date by using random table. Data from medical records of each patient included age, sex, race, date of birth, birth weight (BW), gestational age (GA), place of birth, mode of delivery. Apgar score, prenatal complications, underlying diseases, *Klebsiella* colonization and also endotracheal (ET) intubation, intravenous catheterization and paren-

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teral nutrition. Blood components such as fresh frozen plasma, packed red cells, whole blood, and medications including furosemide, phenobarbital and theophylline given were also recorded. The hospital background was mentioned previously (Pengsaa *et al*, 1993).

Statistical methods

Differences between variables were analysed by chi-square and the student's *t* test was used to compare the means of continuous variables. Mantel-Haenszel chi-square test was used in univariate analysis. The risk factors were obtained from multivariate analysis (conditional stepwise logistic regression) using SPSS statistical package.

RESULTS

During the study period from 1987 to 1989, there were 11,255 liveborn infants in the hospital and 1,717 newborn infants were discharged from the neonatal unit. There were 90 cases of *Klebsiella* septicemia, giving an incidence of 4.1/1,000 livebirths and infection rate of 5.25% of discharged cases. The medical records of 28 cases were lost, so only 62 cases of *Klebsiella* septicemia were studied (Table 1). The male : female ratio was 1 : 1.3 and the inborn : outborn infant ratio was 1 : 1.2. Fifty-one cases (82.3%) were low birth weight and 42 cases (67.7%) were less than 37 weeks gestational age. Thirty-three per cent had perinatal asphyxia and 59.7% had prenatal abnormal conditions, such

as maternal fever and premature rupture of membrane for more than 24 hours. Lethargy and thermal instability were the most common signs and symptoms of *Klebsiella* septicemia.

Table 2 shows the characteristics of the study group compared to control group.

From univariate analysis, birth weight < 1,500 g, gestational age < 37 weeks, outborn patients, Apgar score at 1 minute < 7, endotracheal intubation, central venous catheterization, parenteral nutrition, surgery, blood components transfusion, theophylline and furosemide administration and also respiratory problems and severe congenital anomalies which need surgery were the risk factors for *Klebsiella* septicemia when compare to control group (Table 3). After multivariate analysis (conditional stepwise logistic regression), the risk factors for *Klebsiella* septicemia were only endotracheal intubation and central venous catheterization as demonstrated in Table 4.

DISCUSSION

The prevalence rate of nosocomial infection in Thailand is 11.7% and is highest in regional hospitals and most common in intensive care units (Danchaiwittit and Chokloikaew, 1989). The neonatal unit of Srinagarind Hospital experienced repeated outbreaks of *Klebsiella* septicemia from 1987 to 1989. During this period, nosocomial infection was also demonstrated in other wards in the hospital.

Table 1

Baseline data of infants with *Klebsiella* septicemia.

	No. (%)
Total study cases	62
Male: Female = 1 : 1.3	
Inborn : Outborn = 1 : 1.2	
Birth weight < 2,500 g	51 (82.3)
Gestational age < 37 weeks	42 (67.7)
Apgar score < 7 at 1 minute	20 (33.3)
Abnormal prenatal conditions	37 (59.7)

Table 2

Characteristics of infants with *Klebsiella* septicemia and control group.

	Study (n = 62)	Control (n = 62)
Birth weight (g)		
mean ± SD	1,799 ± 701	2,768 ± 682
range	650-3,900	1,080-4,240
Gestational age (wk)		
mean ± SD	33 ± 4	38 ± 2
range	26-42	31-42
Male : Female	1 : 1.3	1 : 0.8
Inborn : Outborn	1 : 1.2	1 : 0.2

Table 3

Univariate analysis of variables in matched case-control.

Variables	A	B	p value	Odds ratio	95% CI
Birth weight (< 1,500 g)	22	0	< 0.001	NC	
Gestational age (< 37 weeks)	35	3	< 0.001	11.67	3.59-61.45
Place of birth (outborn)	28	4	< 0.001	7.00	2.46-28.90
Apgar score 1 minute <7	16	4	< 0.01	4.00	1.34-16.71
Endotracheal intubation	49	1	< 0.001	49.00	6.77-836.86
Central venous catheterization	38	3	< 0.001	12.67	3.91-66.66
Parenteral nutrition	39	0	< 0.001	NC	
Surgery	17	2	< 0.001	8.50	1.96-67.20
Blood components transfusion	36	5	< 0.001	7.20	2.83-25.02
Drug therapy					
Theophylline	14	0	< 0.001	NC	
Furosemide	17	0	< 0.001	NC	
Diagnosis					
Respiratory problems	31	1	< 0.001	31.00	4.23-530.41
Severe congenital anomalies	21	5	< 0.001	4.20	1.58-14.76

A = Matched set with exposed variable in case and non-exposed variable in control

B = Matched set with non-exposed variable in case and exposed variable in control

NV = Not calculable, denominator of O

Table 4

Risk factors associated with *Klebsiella* septicemia in study group compare to control group.

Variable	Odds ratio	95% CI
Endotracheal intubation	31.57*	2.89-343.82
Central venous catheterization	16.99**	1.15-250.37

* p < 0.01

** p < 0.05

Nosocomial infections caused by the *Klebsiella* species were found in 17.2% of all nosocomial infections in Srinagarind Hospital in the years 1987-1988 (Sithikesorn *et al*, 1989).

The rate of neonatal *Klebsiella* septicemia was 5.2% during this three-year period. Forty-two of the 62 studied cases of neonatal *Klebsiella* septicemia died, an overall mortality rate was 67.7%. For the risk factors, after multivariate analysis by conditional stepwise logistic regression, only two variables had statistical significance: endotracheal

intubation (odds ratio 31.57, 95% CI 2.89-343.82) and central venous catheterization (odds ratio 16.99, 95% CI 1.15-250.37).

In the study of one crowded neonatal intensive care unit (Goldman *et al*, 1981) the risk of nosocomial infection was inversely correlated with birth weight, with a 3% increase in the risk of nosocomial infection for every 500/g decrease in birth weight. The risk of nosocomial infection was also associated with patient ductus arteriosus (PDA), surgery (ligation of PDA) and multiple supportive measures such as endotracheal intubation, hyperalimentation and lipid therapy. In a case-control study (McKee *et al*, 1982), using of the central venous catheter was a risk factor for a multiple resistant *Klebsiella pneumoniae* epidemic (p < 0.01).

In the previous studies, *Klebsiella* species were found not only in the GI tract (McKee *et al*, 1982; Saravolatz *et al*, 1984; Chugh *et al*, 1985; Denny *et al*, 1986) but also on the skin, pharynx, umbilicus, genitalia and external ear canal of the patients (Chugh *et al*, 1985; Eriksson *et al*, 1982; Ostfeld *et al*, 1983). Bacterial colonization was reported to increase with hospitalization (Chugh *et al*, 1985; Casewell and Phillips, 1977), antimicrobial therapy

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and the level of patient care required (Casewell and Phillips, 1977). The incidence of *Klebsiella* colonization of the hands of hospital personnel varied from 17.67% (Casewell and Phillips, 1977; Mayhall *et al*, 1980; McKee *et al*, 1982; Chugh *et al*, 1985; Denny *et al*, 1986).

Positive cultures of *Klebsiella pneumoniae* were also taken from ward environments such as ward surfaces, sinks and incubators (Mayhall *et al*, 1980; Chugh *et al*, 1985). The first documentation of nosocomial bacteremia as a major infectious complication of feeding of premature infants with contaminated breast milk was reported (Donowitz *et al*, 1981). The report of an epidemic of necrotizing enterocolitis in Srinagarind Hospital (Kosuwon *et al*, 1990) found no statistically significant difference in possible risk factors but *Klebsiella* colonization was demonstrated in sampled cultures of feeding formula and intravenous infusion fluid.

The reservoir of this virulent organism was most probably the G-I tract of colonized infants with subsequent colonization of the hands of nursing staff over a short period preceding the outbreak (Casewell *et al*, 1977, Weinstein 1980; Denny *et al*, 1986).

It was noted that multiple incorrect techniques in nursing care could account for inoculation of the pathogens to the oropharynx and upper G-I tract by nursing staff, the hypothesis was supported by recovery of gentamicin resistant *Klebsiella pneumoniae* from culture of nasopharynx and gastric aspirate during the first and second outbreak (Mayhall *et al*, 1980).

As for the risk factors for *Klebsiella* septicemia in this study, it can be concluded that the high risk infants who needed intensive care management might have acquired *Klebsiella* species from the other infants and from inanimate environments. Awareness of these high risk infants by emphasizing cross-infection control measures, prompt identification and isolation of colonized and infected infants will help in successful control of such outbreaks.

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REFERENCES

- Casewell K, Phillips I. Hands as route of transmission for *Klebsiella* species. *Br Med J* 1977; 2 : 1315-7.
- Chugh TD, Ghaffoor SA, Kuruvilla AC, Bishbishi EA. Colonization and infections of neonates by *Klebsiella pneumoniae* in an intensive care unit. *J Trop Pediatr* 1985; 31 : 200-3.
- Danchaivijitr S, Chokloikaew S. A national prevalence study on nosocomial infections 1988. *J Med Assoc Thai* 1989; 72 (suppl 2) : 1-6.
- Denny F, St. John MA, Lewis DB, Daniel B. Nosocomial *Klebsiella pneumoniae* colonization in a neonatal special care unit. *Ann Trop Paediatr* 1986; 6 : 123-6.
- Donowitz LG, Hally CE, Gregory WW, *et al*. Neonatal intensive care unit bacteremia : emergence of gram-positive bacteria as major pathogens. *Am J Infect Control* 1987; 15 : 141-7.
- Donowitz LG, Marsik FJ, Fisher KA, Wenzel RP. Contaminated breast milk : a source of *Klebsiella* bacteremia in a newborn intensive care unit. *Rev Infect Dis* 1981; 3 : 716-20.
- Eriksson M, Melen B, Myrback K-E, Winbladh B, Zetterstrom R. Bacterial colonization of newborn infants in a neonatal intensive care unit. *Acta Paediatr Scand* 1982; 71 : 779-83.
- Freeman J, Epstein MF, Smith NE, *et al*. Extra hospital stay and antibiotic usage with nosocomial coagulase-negative staphylococcal bacteremia in two neonatal intensive care unit populations. *Am J Dis Child* 1990; 144 : 324-9.
- Goldman DA, Durbin WA Jr, Freeman J. Nosocomial infection in a neonatal intensive care unit. *J Infect Dis* 1981; 144 : 449-59.
- Hable KA, Matsen JM, Wheeler DJ, *et al*. *Klebsiella* type 33 septicemia in an infant intensive care unit. *J Pediatr* 1972; 80 : 920-4.
- Kosuwon P, Lumbiganon P, Sutra S, Pairojkul S, Taksaphan S. Neonatal necrotizing enterocolitis outbreak in a nursery ward : analysis of some risk factors. *J Pediatr Soc Thai* 1990; 29 : 11-20.

- Mayhall CG, Lamb VA, Bitar CM, *et al.* Nosocomial *Klebsiella* infection in a neonatal unit : identification of risk factors for gastrointestinal colonization. *Infect Control* 1980; 1 : 239-46.
- McKee KT Jr, Cotton RB, Stratton CW, *et al.* Nursery epidemic due to multiply-resistant *Klebsiella pneumoniae*: epidemiologic setting and impact on perinatal healthy care delivery. *Infect Control* 1982; 3 : 150-6.
- Ostfeld E, Segal J, Segal A, Bogokovski B. Bacterial colonization of the nose and external ear canal in the newborn infants. *Israel J Med Sci* 1983; 19 : 1046-9.
- Pengsaa K, Lumbiganon P, Taksaphan S, *et al.* Do sterile gloves reduce nosocomial infection in the neonatal ward? *J Infect Dis Antimicrob Agents* 1993;10: 1-7.
- Saravolatz LD, Arking L, Pohlod D, Fisher EJ, Borer R. An outbreak of gentamicin-resistant *Klebsiella pneumoniae* : analysis of control measures. *Infect Control* 1984; 5 : 79-84.
- Sidebottom DG, Freeman J, Platt R, *et al.* A fifteen years experience with blood stream isolates of coagulase-negative staphylococci in neonatal intensive care. *J Clin Microbiol* 1988; 26 : 713-8.
- Sithikesorn J, Lumbiganon P, Bunma P, Patjanasuntorn B. Nosocomial infections in Srinagarind Hospital. *J Med Assoc Thai* 1989; 72 (suppl 2) : 12-4.
- Weinstein RA. Endemic aminoglycoside resistance in gram negative bacilli : epidemiology and mechanisms. *J Infect Dis* 1980; 14 : 338-45.