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Risk Factors for Neonatal Infections in Full-term Babies in South Korea

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Purpose: Since 1997, private postnatal care facilities (San-hu-jo-ri-won in Korean) have emerged to take the role of the family. As a result, neonates are now exposed to many people and are very vulnerable to infection. However, there has been no study on the influence of postnatal care facilities on neonatal infection. The aim of this study was to determine the risk factors of neonatal infection in full-term babies in Korea. **Materials and Methods:** We followed up 556 pregnant women and their babies for 4 weeks after their births at 2 hospitals in Seoul and Daejeon from October 2004 to September 2005. Among 512 full-term babies, 58 had infectious diseases. To determine the risk factors for infection, 53 infected neonates at 4 - 28 days of life and 413 healthy neonates were compared. **Results:** The incidence of neonatal infection at 4 to 28 days after birth was 10.5%. After adjusting the related factors, the number of siblings (OR = 2.05, 95% CI = 1.13 - 3.71 for 1 or more) and postnatal care facilities or home aides (OR = 1.91, 95% CI = 1.07 - 3.45) were significant risk factors. Formula or mixed feeding (OR = 1.66, 95% CI = 0.91 - 3.04) increased the risk of neonatal infection but it was not statistically significant. **Conclusion:** When the newborns had siblings, stayed at postnatal care facilities, or were cared for by home aides, the risk of neonatal infections significantly increased. Further research on the feeding effect on neonatal infection and evaluation of prevention efforts are needed.

Key Words: Infant, newborn, infection, cohort study, postnatal care, facilities, home health aides

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INTRODUCTION

Neonatal infection is a problem occurring in less than 4% of infants, however, it has different severity.[1] Neonatal sepsis and meningitis are the most severe invasive diseases among neonatal infections, and are critical determinants of mortality and morbidity.[2] Even the most relatively mild common infections diagnosed and treated by pediatricians are burdensome for the babies' families. Understanding the incidence and distribution of these mild infections contributes to better utilization of health resources and antibiotics during the neonatal period. However, the literature on neonatal infection after nursery discharge is scare.

According to World Health Organization (WHO) estimates, there were about 5 million neonatal deaths in 1995, 98% of which occurred in less developed countries.[3] The number of neonatal deaths decreased to 4 million in 2005, but 98% still occurred in less developed countries.[4] Among them, infection was a main cause.[5-7]

Neonatal infection can be acquired in utero, during the birth process, or soon after birth. Not all types of neonatal infections are apparent at birth but may manifest with signs of disease in weeks, months, or years. After birth, neonates are exposed to infectious agents in nurseries or community. Postnatal infections may be transmitted by direct contact with hospital personnel, mothers, family members, breast milk, or various inanimate sources. In Korea, postnatal care for the mother and newborn baby was traditionally carried out at home by all family members including maternal and paternal grandmothers to prevent neonatal infections. Newborn infants were isolated from

other children or visitors until at least 21 days after birth. Traditional postnatal care gradually disappeared and a new postnatal care method became popular. Since 1997, Postnatal care Facilities (San-hu-jo-ri-won in Korean) have taken the role of the family.[8] Neonates are now exposed to many people, and are very vulnerable to infection under the care of the special facilities. However, there has been no study on the risk factors of neonatal infection including the influence of postnatal care facilities. Thus, we carried out this study to evaluate the incidence, risk factors, and characteristics of neonatal infections in the first month of life.

MATERIALS AND METHODS

Population and definitions

This study included infants who were born at 2 neonatal centers in Seoul and Daejeon from October 2004 to September 2005. The neonatal center in Daejeon is a level III center and the center in Seoul is level II (level I is for clinics, levels II and III are for general hospitals, and level III is for last referral centers). All participating centers are located in training hospitals and have neonatology specialists.

Neonatal infection was defined by babies' history of infections diagnosed by doctors at day 4 - 28 of life.

Feeding type and baby sitters in the first month of life were surveyed. We grouped feeding type by breast feeding only, formula feeding only, and mixed feeding. Those who used breast and formula feeding from the first day of birth and those who used breast feeding during the first or second week and switched to formula or mixed feeding were included in the mixed feeding group.

For baby care, there are different kinds of care givers: the parents, grandparents, home health aides, and staff at postnatal care facilities. Home health aides (home aides) are those who assist the ill, elderly, or disabled at their homes, carrying out personal care and housekeeping tasks. Postnatal care is a type of care provided for a mother following the birth of a child. Some mothers stayed at postnatal care facilities during the first or second week and were later cared for by their families. We grouped baby care type by family only, home aides (if they used home aides for 1 or more days), and postnatal care facilities (if they used postnatal care facilities for 1 or more days).

We identified 556 mothers who visited Eulji University Hospital in Seoul and Daejeon from October 2004 to September 2005 for group B streptococcus study at 35 - 37 weeks of gestation and they agreed to participate in the study. Of these, 14 mothers who delivered at other hospitals, 22 newborns who could not be followed up at 4 weeks after birth, and 12 newborns who were less than 37 weeks of gestation were excluded from the cohort. Among 512 eligible newborns including 4 twins, 413 had no diseases, 41 had non-infectious diseases, and 58 had infectious diseases. Five babies were excluded because of infection that occurred within 3 days after birth. As a result, 53 cases were grouped as infected neonates. Neonatal sepsis was diagnosed clinically or via positive blood or cerebrospinal fluid (CSF) culture. A group of healthy neonates included infants who had no diseases among babies of the pregnant women's cohort (413 newborns).

To reduce misclassification bias, if doctors did not diagnose the illness as an infectious disease, babies were not included in the infected neonates group even if they had some symptoms (Fig. 1).

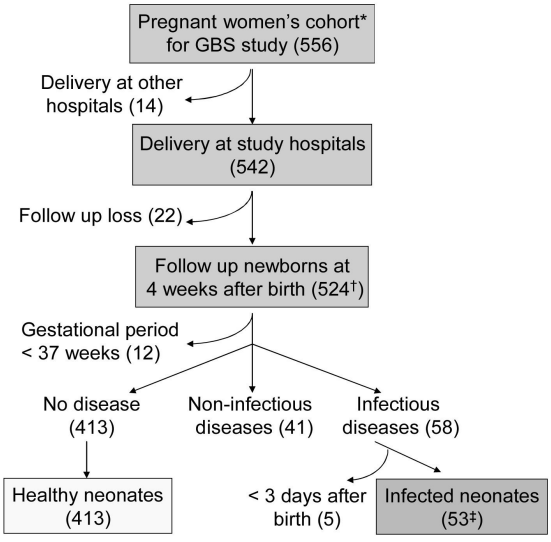

Fig. 1. Flow chart of data collection. *Gestation period 35 - 37 weeks. †Four twins were included. ‡One twin was included.

Data collection

We surveyed pregnant women at 35 - 37 weeks for group B streptococcus study and followed up 4 weeks after delivery. Face-to-face interviews were conducted when mothers visited hospitals for BCG vaccination. For mothers who did not visit hospitals, we carried out telephone surveys. Medical charts of all mothers and babies were reviewed for perinatal characteristics and related factors such as gender, gestational age, birth weight, 1- and 5-minute Apgar scores, delivery methods, and prolonged rupture of membranes (PROM). We surveyed mothers for medical history of babies, baby care, postnatal care, and feeding type for the first month of life. Two trained research nurses in Seoul and Daejeon interviewed study subjects, collected medical and feeding data using Excel software, followed by confirmation from a researcher. This study was approved by the Institutional Review Board (IRB) of Eulji University Hospital.

Data analysis

The incidence of neonatal infection was calculated by dividing the number of infants with infection between 4 and 28 days after birth by the total number of followed newborns minus the number of infants with infection within 3 days after birth. Therefore, the numerator was 53 infected cases and denominator was 507 (53 infected cases + 41 non-infectious cases + 413 healthy neonates).

Because feeding and baby care type can change day by day, we surveyed the factors in chronological order and only histories that occurred before disease onset were included in the analysis.

We used chi-square test to assess associations between known and hypothesized risk factors and neonatal infection. Multiple logistic regression models were used to assess associations between neonatal infection and environmental characteristics of babies. All p values were 2-sided, and p values less than 0.05 were considered statistically significant. Analyses of clustered data were performed using SPSS version 14.0 (SPSS Inc., Chicago, IL, USA).

RESULTS

Incidence of neonatal infection

Between October 2004 and September 2005, 512 full-term babies were followed at 4 weeks after birth. Of these babies, 53 had infectious diseases at days 4 - 28 of life. The incidence of neonatal infection (4 - 28 days) in full-term babies was 10.5%. The most common infection was upper respiratory infection (5.32%) and the second most frequent infection was gastroenteritis (2.56%). Conjunctivitis (0.99%), neonatal sepsis (0.79%), pneumonia (0.39%), and omphalitis and skin infection (0.39%) followed (Table 1).

Risk of neonatal infection

We evaluated related factors of neonatal

Table 1. Incidence of Neonatal Infection between 4 and 28 Days after Birth in Full-term Babies

	n (%)	Incidence (%)*
Upper respiratory infection	27 (50.9)	5.32
Gastroenteritis	13 (24.5)	2.56
Conjunctivitis	5 (9.4)	0.99
Neonatal sepsis	4 (7.5)	0.79
Pneumonia	2 (3.8)	0.39
Omphalitis and skin infection	2 (3.8)	0.39
Total	53 (100)	10.5

*Denominator = 507.

infection according to their nature, such as prenatal vs. postnatal. Prenatal factors such as the mother's age and education level, location of birth hospital, and gender of the baby were not significantly different between infected and healthy neonates (Table 2).

Among postnatal factors, the distribution of proportion was significantly different by feeding type ($p = 0.015$), and the trend showed significant results by the number of siblings ($p = 0.034$) and baby care type ($p = 0.031$) (Table 2).

The risk of infection increased by the number of siblings. When no sibling was reference, newborns with 1 or more siblings showed a risk ratio 1.99 times higher. Compared to breast feeding, formula or mixed feeding showed a risk ratio of 1.60 but it was not statistically significant. Compared to a family-cared baby, the risk ratio of infection increased by 1.91, if the baby was cared for in postnatal care facilities or by a home aide, and it was statistically significant (Table 3).

To adjust for related factors, multiple logistic regression models were applied. The last model included baby care type, feeding type, and number of siblings. After adjusting for those factors, the number of siblings was shown to increase the risk ratio (OR = 2.05, 95% CI = 1.13 - 3.71). Baby care by workers at postnatal care facilities or home aides (OR=1.92, 95% CI = 1.07 - 3.45) also increased the risk of neonatal infection. Formula or mixed feeding showed increased risk (OR = 1.66, 95% CI = 0.91 - 3.03) but it was not significant (Table 3).

DISCUSSION

Among full-term babies, the incidence rate of

Table 2. Related Factors of Neonatal Infection in Full-term Babies (%)

		Infected neonates (n = 53)	Healthy neonates (n = 413)	p value*
Mothers' age	(yrs, mean ± SD)	31.34 ± 3.595	31.37 ± 3.669	0.950
Mothers' education level	≤ High school	30.2	40.7	0.141
	≥ College	69.8	59.3	
Region of birth hospital	Daejeon	24.5	36.6	0.084
	Seoul	75.5	63.4	
Gender of baby	Girls	47.2	50.1	0.686
	Boys	52.8	49.9	
No. of siblings	0	37.7	54.7	0.034†
	1	52.8	38.3	
	2+	9.4	7.0	
Feeding type‡	Breast feeding	35.8	47.2	0.015
	Mixed feeding	54.7	34.8	
	Formula feeding	9.4	18.0	
Baby care type‡	Family	43.4	59.4	0.031†
	Home aides	9.4	7.1	
	Postnatal care facilities	47.2	33.6	

*p values obtained by Chi-square test.
†p values obtained by trend test.
‡No. of unknown cases in healthy neonates were two in feeding type and one in baby care type.

Table 3. Risk of Neonatal Infection by Using a Multiple Logistic Regression Model

Variables of regression model		Infected neonates n (%)	Healthy neonates n (%)	Unadjusted OR	Adjusted OR (95% CI)
No. of siblings	0	20 (37.7)	226 (54.7)	1.00	1.00
	1+	33 (62.3)	187 (45.3)	1.99	2.05 (1.13 - 3.71)
Baby care	Family	23 (43.4)	244 (59.4)	1.00	1.00
	Postnatal care facilities or home aids	30 (56.6)	167 (40.6)	1.91	1.92 (1.07 - 3.45)
Feeding type	Breast feeding	19 (35.8)	194 (47.2)	1.00	1.00
	Formula feeding or mixed feeding	34 (64.1)	217 (52.8)	1.60	1.66 (0.91 - 3.03)

community-acquired neonatal infection was 10.5% (53/507). The potent risk factors for neonatal infection were the numbers of siblings and baby care at postnatal care facilities.

After birth, newborns may become infected by various pathways involving human carriers or contaminated materials and equipment. Neonatal infection could be categorized according to 5 sources: 1) congenital infections with onset in utero, 2) infections acquired during the birth process from the maternal genital tract, 3) infections acquired in the nursery, 4) infections acquired in the household after discharge from the nursery, and 5) infections suggesting an anatomic defect, underlying immunologic disease, or metabolic abnormality.[9] All types of infection sources can induce signs of infection in the first weeks or months of life. If signs of infectious diseases develop in infants who were well when they were discharged from the nursery and whose gestation and delivery did not involve significant risk factors, the infection is highly likely to have been acquired from a household or community member. Newborns are susceptible to many infectious agents that are colonized from other members of the household and caregivers. A detailed history of illness of family members can suggest the source of the disease.

In Korea, postnatal care facilities have been popular since 1997. Non-medical people can establish and manage the facilities, and there are no established standards, continuously causing many outbreaks. As a result, guidelines for postnatal care facilities were released in 2002.[10] According to the guidelines, the distance between 2 babies should be more than 1.5 m, space for 1 baby should be more than 1.7 m^2, and 1 worker can care for a maximum of 8 babies. However, these limited guidelines do not have any binding power. In our data, 35.1% of pregnant women used postnatal care facilities, which rate was not different from the Korean national data. Despite the high frequency of outbreak reported by the mass media,[11] there have been few studies on this issue. Kim et al. reported severe gastroenteritis neonatal cases transferred from postnatal care facilities and suggested the possibility of neonatal infection source,[12] and Yoo et al. pointed out the necessity of legal basis and education for facility workers.[13] The present study also showed home aides(OR = 1.83) and postnatal care facilities(OR = 1.92) increased the risk of infection. However, the number of cases who were under home aide care was low, and we could not find significant differences between home aides and postnatal care facilities.

There is much evidence for immunologic advantages of breast feeding in preventing infection.[14] A recent study focused on the duration of exclusive breast feeding necessary to confer protection against infection during infancy.[15] However, there is little published evidence to support the role of breast feeding in the prevention of community-acquired neonatal infections.

Among studies on breast feeding and respiratory infection, 1 report described a protective role of breast feeding and suggested a mechanism of breast feeding in infection prevention. Breast milk, especially colostrum, is rich in cellular and acellular factors that could be important to neonatal respiratory immunity:[16] reduced risk of infection was shown in the exclusive breast feeding group compared to the mixed or formula feeding group. Regarding mixed feeding, it is difficult to measure the amount of breast and formula feeding separately. Moreover, the number of cases with formula feeding only was very low. Therefore, we could not differentiate the effect of mixed feeding from that of formula feeding only.

The number of siblings is a well-known risk factor of neonatal infection, and we found similar results. A large number of siblings increased the risk of neonatal infection compared to the no-sibling group, and the risk ratio increased by 2.05 for the 1 sibling or more group. However, the number of cases with 2 or more siblings was very low, and we could not find the dose-response relationship. Although several studies found no relationship between neonates with sibling visitation and bacterial colonization,[17-20] increased infection rate is more likely to be associated with viral infection from siblings than bacterial infection. Upper respiratory infectious disease was the most common morbidity cause in the present study, transmitted by airborne route. However, the present study had limitations in examining the effect of siblings on neonatal infection. We only examined the existence and number of siblings, not their health.

This is a cohort study, and subjects were all from pregnant women's cohort. There was no selection bias between the group compared. However, because of the characteristics of related factors such as feeding type and baby care, we surveyed the related factors after the outcome onset, and recall bias can arise. To reduce recall bias, interviews were carried out within 4 - 6 weeks after birth. The number of cases was not enough to differentiate the effect of breast feeding, but it was enough to evaluate the risk of postnatal care facilities, which was the objective of this study.

In conclusion, the incidence rate of neonatal infection in full-term babies in Korea was about 10.5%. We confirmed the known risk factor for neonatal infection, the number of siblings. Separation of newborns from young siblings to prevent neonatal infection needs to be emphasized to mothers. Furthermore, we found new risk factors; postnatal care facilities and home aides. To decrease the incidence of neonatal infection, standards of hygiene for postnatal care facilities need to be established and should be more closely supervised by the government. Further research on the effect of mixed feeding on neonatal infection and evaluation of prevention efforts are needed.

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