Published in final edited form as:
Pediatr Infect Dis J. 2005 July ; 24(7): 586–589.

Epidemiology and Diagnosis of Hospital-Acquired Conjunctivitis Among Neonatal Intensive Care Unit Patients

Janet Haas, RN, MS[*,†], **Elaine Larson, PhD, RN**[*], **Barbara Ross, RN, BSN**[‡], **Benjamin See, SM (ASCP), MS,**[§], and **Lisa Saiman, MD, MPH**[†,||]

[*]*Columbia University School of Nursing, New York, NY*

[†]*Department of Epidemiology, NewYork-Presbyterian Hospital Columbia University Medical Center, New York, NY*

[‡]*Department of Epidemiology, NewYork-Presbyterian Hospital Weill Cornell Medical Center, New York, NY*

[§]*Department of Microbiology, NewYork-Presbyterian Hospital Weill Cornell Medical Center, New York, NY*

[||]*Department of Pediatrics, Columbia University Medical Center, New York, NY*

Abstract

Background: Few recent reports describe the epidemiology and risk factors for health care-associated conjunctivitis among neonatal intensive care unit (NICU) patients in developed countries. Reporting may be inaccurate in this population given that the National Nosocomial Infection Surveillance System (NNIS) definition is largely dependent on a positive culture, whereas clinical practice often consists of empiric treatment.

Objectives: We describe the epidemiology of conjunctivitis among neonates in 2 level III–IV NICUs and compare the NNIS definition with our study definition: eye drainage and empiric treatment with or without a culture.

Methods: Patient demographics, clinical, device usage and conjunctivitis data collected prospectively from March 2001 through January 2003 were analyzed.

Results: Conjunctivitis occurred in 5% (n = 154/2935) of infants, of whom 51% (n =79) were in NICU 1 and 49% (n =75) in NICU 2. Predominant pathogens included coagulase-negative staphylococci (25%), *Staphylococcus aureus* (19%) and *Klebsiella* spp. (10%). Significant predictors of conjunctivitis included low birth weight, use of ventilator or nasal cannula continuous positive airway pressure and study year. Ophthalmologic examination was an additional predictor of infection in NICU 1. Eye examination data were unavailable for NICU 2. Only 62% of cases that met the study definition for conjunctivitis met the NNIS definition, because many infants received empiric treatment.

Conclusions: Clinical conjunctivitis was associated with low birth weight and patient care factors that could lead to contamination of the eye with respiratory tract secretions. The NNIS definition failed to detect 38% of clinical infections. Consideration should be given to revising the definition of conjunctivitis for the NICU population.

Keywords

conjunctivitis; neonatal intensive care unit; low birth weight; premature infants

Conjunctivitis is one of the most frequently occurring health care-acquired (HA) infections in the neonatal intensive care unit (NICU), but there are few recent reports describing the epidemiology of this clinical entity.[1] Conjunctivitis develops in neonates because of their immature lacrimal duct systems, immature immune systems, and because colonization of the conjunctivae can occur during neonatal care. HA conjunctivitis is defined as occurring 48 hours or more after hospitalization and is caused by bacterial or viral pathogens unrelated to maternal infection. Conjunctivitis can often be treated effectively with topical antimicrobial agents without further sequelae; thus these infections are often treated empirically without obtaining cultures.

Although surveillance is essential to discern the rate of conjunctivitis, to determine factors that may be associated with infection and to plan and evaluate prevention strategies, reporting may be inaccurate because of potential inadequacies in case definitions or surveillance protocols. The National Nosocomial Infection Surveillance (NNIS) system has established standardized definitions of health care-acquired infections, including conjunctivitis, that are widely used,[2] but the NNIS definition relies on culture results or signs and symptoms not likely to be exhibited in the NICU population. Although erythema may be reported in this population, pain in or around the eye is rarely described in NICU patients. Thus the purposes of this study were to describe the epidemiology of health care-acquired conjunctivitis among infants hospitalized in the NICU and to compare the current NNIS definition of conjunctivitis with a broadened study definition that included clinical signs of infection that were treated empirically.

MATERIALS AND METHODS

Sample and Setting.

This substudy was part of a 2-year study to assess the impact of hand hygiene regimens on HA infection among infants hospitalized in the NICU. The hand hygiene regimens used were an alcohol-based hand antiseptic (61% ethanol alcohol) or a 2% chlorhexidine-containing soap product. The study was conducted from March 1, 2001 through January 31, 2003. The study sites were 2 level III–IV NICUs in New York City. NICU 1 was a 43-bed tertiary care unit where 1682 patients were admitted for >24 hours during the study period and accounted for 28,158 patient-days. NICU 2 had 50 beds, and 1244 neonates accounted for 23,220 patient-days. Data were collected prospectively on all infants and included demographic data (eg, birth weight and gestational age), procedures (eg, surgery), device utilization [eg, days of nasal cannula continuous positive airway pressure (NC-CPAP) and mechanical ventilation], and medications (eg, use of antibiotics or parenteral nutrition). In NICU 1, data regarding the number of eye examinations performed to assess retinopathy of prematurity (ROP) were available and were included as a potential risk factor. Eye examinations performed for suspected infections were not included.

Case-Finding Procedures.

Infection surveillance was conducted by an infection control professional (ICP) hired specifically for this study. Because clinicians in NICU 2 reported that eye cultures for suspected conjunctivitis were not routinely obtained, the definition of conjunctivitis used in the study included drainage from the eye and empiric treatment with antibiotics and/or growth of a known pathogenic organism (eg, *Staphylococcus aureus*, *Pseudomonas aeruginosa*) from cultures obtained from purulent drainage and/or the conjunctiva. Case-finding included review of computerized microbiology reports as well as chart review and interviews with patient care providers.

Comparison of Surveillance Methods.

Cases of conjunctivitis identified in this study were independently reviewed by the study ICP and a hospital ICP to assess how frequently the cases identified by the study definition fulfilled the NNIS definition for conjunctivitis. The NNIS definition of HA conjunctivitis is as follows: no signs or symptoms of conjunctivitis occurring within 48 hours of admission; pathogens are cultured from purulent exudate obtained from the conjunctiva or contiguous tissues; or pain or redness of conjunctiva or area around the eye and at least 1 of the following signs of infection: white blood cells and organisms seen on Gram-stained smear of exudate; purulent exudate; positive antigen test; multinucleated giant cells seen on microscopic examination of conjunctival exudates.

Microbiologic Procedures.

Eye cultures were collected by nursing staff when clinically indicated. No surveillance cultures were obtained for this study. Nurses gently swabbed the infants' conjunctivae with a Culturette swab (Becton Dickinson Microbiology Systems, Sparks, MD). The swabs were sent to the microbiology laboratories of each respective institution and inoculated onto trypticase soy agar with 5% sheep blood or Columbia CNA with 5% sheep blood, chocolate and MacConkey commercial agar plates (Becton Dickinson). Plates were incubated in an aerobic environment with 5% added CO_2 at 35°C and examined daily for the detection of bacterial growth for 3 days. Gram-stained smears were also prepared for preliminary examination. Organisms were identified by the automated systems MicroScan (West Sacramento, CA) in NICU 1, or Vitek 2 (bioMérieux, Durham, NC) in NICU 2 and by conventional biochemical tests. Susceptibility testing was performed in accordance with the National Committee for Clinical Laboratory Standards (Wayne, PA) by either the Vitek 2 or MicroScan system or by the conventional agar disk diffusion method. Cultures were not routinely sent for viral pathogens or *Chlamydia*.

Data Analysis.

Data were analyzed using SPSS version 11.5 (SPSS, Inc., Chicago, IL). The relationship between first episode of conjunctivitis and several predictor variables was assessed using χ^2 or Student *t* tests as appropriate. Variables included demographic data as well as device utilization, and whether the device was used for greater than the mean duration for the study population. Variables significant at $P \leq 0.05$ were then entered into a logistic regression model to identify predictor variables that remained significant.

RESULTS

Incidence of Conjunctivitis.

At least 1 episode of conjunctivitis was diagnosed in 5% (n = 154) of 2935 infant admissions during the study period, of whom 51% (n = 79) and 49% (n = 75) were in NICUs 1 and 2, respectively. The demographics of the patients are shown in Table 1. There were some differences in patient populations between the 2 NICUs. Mean gestational ages were 34.7 and 35.1 weeks in NICUs 1 and 2, respectively ($P = 0.09$). Mean birth weights were 2389 and 2447 g, respectively ($P = 0.08$); significantly more neonates weighed <1000 g in NICU 1 than in NICU 2 (12.8% versus 8.7%; $P < 0.01$). NICU 1 had significantly higher device utilization ratios for NC-CPAP (0.37 versus 0.08; $P < 0.001$).

Overall 26% (n = 40) of cases were caused by Gram-positive pathogens and 24% (n = 37) by Gram-negative pathogens, in 29% (n = 44) of cases >1 organism was cultured and 21% (n = 33) had either no growth or were not cultured. As summarized in Table 2, the predominant pathogens treated included coagulase-negative *Staphylococcus* (CoNS) (25%), *S. aureus* (19%), *Klebsiella* spp. (10%) and *P. aeruginosa*, *Serratia marcescens*, and *Escherichia coli*

(8% each). As predicted by the clinical practices described above, the culturing patterns varied by NICU; 96% of the cases of conjunctivitis diagnosed in NICU 1 had accompanying cultures, compared with 59% in NICU 2 ($P < 0.001$). In addition, the number of cases of conjunctivitis identified in both NICUs increased from year 1 to year 2 of the study. In NICU 1, 30 cases of conjunctivitis were identified in year 1, and 48 cases were identified in year 2. Similarly NICU 2 identified 31 cases in year 1 and 45 cases in year 2. There was no significant difference in reporting between NICUs ($P > 0.05$).

In the univariate analysis, significant predictors of conjunctivitis included low birth weight, use of NC-CPAP ($P = 0.02$), ventilator use ($P < 0.001$) and year of study ($P = 0.03$). Gender, hand hygiene regimen and study site were not significant cant predictors of conjunctivitis. Low birth weight, use of NC-CPAP for >2.9 days, use of a ventilator for >4.3 days (which were the mean durations of use of these devices in the study population) and year of study were significantly associated with conjunctivitis in the logistic model (Table 3).

Risk factors in NICU 1 were analyzed separately to include eye examination for ROP as a predictor of conjunctivitis. Eighteen percent (14 of 79) of case infants had at least 1 eye examination before infection, compared with 7% (115 of 1615) of noncase infants ($P < 0.001$). Among the cases, 71% (10 of 14) had an examination within 1 week before the diagnosis of conjunctivitis. Logistic regression demonstrated that the risk of conjunctivitis was 3.7 (95% confidence interval, 1.8, 7.4) times higher among infants who had at least 1 prior eye examination, compared with those who had not. Birth weight, use of mechanical ventilation and NC-CPAP for >2.9 and 4.3 days, respectively, the mean use for our study population, remained significant predictors of conjunctivitis in this model (Table 4).

Comparison of Surveillance Methods.

Only 62% of cases defined by study criteria for conjunctivitis fulfilled the NNIS definition. As expected, the NNIS surveillance definition for conjunctivitis failed to detect a substantial proportion (38%) of cases. Whereas 100% conjunctivitis cases had documented drainage from 1 or both eyes, only 1.9% (n = 3) had redness and swelling documented in the medical record. As predicted, empiric treatment or bacterial culture were the main diagnostic criteria for conjunctivitis.

DISCUSSION

There are few descriptions of the epidemiology of HA conjunctivitis in patients hospitalized in the NICU, particularly in the modern era.[3] This study was one of the largest studies conducted recently to examine endemic conjunctivitis in NICUs. Conjunctivitis affected 5% of neonates in this study, consistent with other reports in which conjunctivitis rates ranged from 1.6 to 12% of neonates.[4–7] These previous studies were performed among infants in a well baby nursery, maternity wards or did not specify whether infants from NICUs were included. In addition, cultures for viruses and *Chlamydia* were also included.

In our study, low birth weight was a consistent and significant independent predictor of conjunctivitis. Conjunctivitis may develop more frequently in premature infants because these infants spend considerable time with their eyes closed or covered, which allows bacteria to proliferate, and because of immature lacrimal system.[8] A functional lacrimal system produces tear components, opening and closing of the eyelids act as a pump to facilitate tear distribution across the surface of the eye and the lacrimal ducts act as a drainage system, which carries away tears, epithelial debris and bacteria. However, the lacrimal ducts are not patent in 20% of full term neonates, and nonpatent ducts may be more frequent in premature infants.[9] Nonpatent lacrimal ducts allow bacteria, tears and other debris to pool on the surface of the eye and provide a medium for bacterial growth.

We also demonstrated an association between conjunctivitis and respiratory support including NC-CPAP, endotracheal intubation and mechanical ventilation. The respiratory care required for infants needing ventilatory assistance may allow respiratory secretions to be transferred from the nasopharynx to the eyes, particularly during suctioning. In a study of an outbreak of *P. aeruginosa* conjunctivitis in a pediatric hospital, 70% of patients from whom respiratory cultures were obtained before the onset of conjunctivitis were colonized with this organism.[10] In this previous study, all case patients had respiratory interventions such as the use of an endotracheal tube or suctioning preceding conjunctivitis.

Another factor significantly associated with conjunctivitis was the year of study. The second year of study was associated with a higher rate of conjunctivitis and may represent better case-finding and improved documentation of drainage from the eyes as the study progressed. This finding was consistent between the 2 NICUs. Despite better case-finding and documentation, 38% of the conjunctivitis cases identified by our study definition were not diagnosed by the NNIS definition. In settings such as NICU 2, in which eye drainage is treated empirically, cases may fail to meet the NNIS definition of conjunctivitis because cultures are not routinely obtained. Such NICUs may report lower rates of infection than those in which cultures were obtained from suspected cases of conjunctivitis. Our broader study definition and prospective chart review of all neonates allowed us to identify clinically defined cases of conjunctivitis, which increased the rate of conjunctivitis relative to the NNIS definition.

The organisms most commonly causing conjunctivitis in our population were CoNS and *S. aureus*, followed by the Gram-negative pathogens *Klebsiella* spp., *P. aeruginosa*, *Serratia marcescens* and *E. coli*. Our findings are consistent with previous reports in the medical literature.[4–6] However, conjunctival colonization is very common in neonates.[11,12] Studies have reported positive surveillance cultures of conjunctivae in NICU patients in the absence of clinical signs and symptoms of conjunctivitis, and some clinicians have suggested that eye cultures have little utility in the diagnosis of conjunctivitis.[11,13] In a recent surveillance study of conjunctival colonization among NICU patients, 58% of patients in NICUs had at least 1 positive conjunctival culture, and 75% of isolates were CoNS.[11] Furthermore asymptomatic infants were as likely to have negative cultures as those infants with conjunctival edema, erythema or exudates.[11]

There were some limitations to this study. Our definition of conjunctivitis depended on complete documentation of signs and symptoms. It is probable that some cases were missed because of incomplete documentation of signs and symptoms. In contrast, the increased rate of conjunctivitis during the second year of the study may have been caused by more diligent documentation of signs and symptoms by the NICU staff as the study progressed. In addition, it may be difficult to distinguish colonization from true infection in this population. Our study definition may have included some infants who were treated for a noninfectious etiology of conjunctivitis. Finally patients whose symptoms resolved without the use of antibiotics were not included in this study.

Our study assessed factors associated with the development of health care-acquired conjunctivitis among NICU patients. Low birth weight, greater duration of mechanical ventilation, greater duration of NC-CPAP and eye examinations for ROP were risk factors for conjunctivitis. These findings have important implications because some of these risk factors can be modified by strict adherence to infection control techniques. Protecting the eyes of intubated infants during respiratory care and frequent assessment of nasal prong placement while patients are receiving NC-CPAP therapy may reduce contamination of the eyes with respiratory secretions. During eye examinations, adherence to strict aseptic technique including the use of eye drops in single dose vials when available and assurance of an adequate supply of sterile instruments can decrease the risk of conjunctivitis.

Because many institutions treat symptomatic eye infections empirically without culture, we suggest that a more inclusive definition of conjunctivitis from NNIS is indicated. In addition, the rates for conjunctivitis should be published more frequently so that hospitals can use the NNIS rate as a relevant benchmark. Although many hospitals might consider surveillance for HA conjunctivitis a lower priority than surveillance for more invasive diseases, a benchmark for comparison would be very helpful if an outbreak was suspected. With strict attention to infection control practices and a relevant benchmark for comparison, interventions to decrease conjunctivitis in this vulnerable population can be implemented and assessed.

ACKNOWLEDGMENTS

We gratefully acknowledge the contributions of Pablo San Gabriel, Osode Coki and Ari Allen in the preparation of the manuscript.

Supported in part by grant 1RO1 NR05 197 (“Staff Hand Hygiene Practices and Nosocomial Infections in Neonates.”) from the National Institute for Nursing Research, National Institutes of Health.

REFERENCES

1. Maderova E, Kestnerova V, Cervenka J, Pucekova C. Prevalence of nosocomial infections in selected hospitals. J Hyg Epidemiol Microbiol Immunol 1987;31:365–374.
2. Emori TG, Culver DH, Horan TC, et al. National Nosocomial Infections Surveillance System (NNIS): description of surveillance methods. Am J Infect Control 1991;19:19–35. [PubMed: 1850582]
3. Jang TN, Fung CP, Yang TL, Shuen SH, Huang CS. Use of pulsed-field gel electrophoresis to investigate an outbreak of *Serratia marcescens* in a neonatal intensive care unit. J Hosp Infect 2001;48:13–19. [PubMed: 11358466]
4. Hammerschlag M. Neonatal conjunctivitis. Pediatr Ann 1993;22:346–351. [PubMed: 8414687]
5. Fransen L, Van den Berghe P, Mertens A, Van Brussel K, Clara R, Piot P. Incidence and bacterial aetiology of neonatal conjunctivitis. Eur J Pediatr 1987;146:152–155. [PubMed: 3569352]
6. Pandey KK, Bhat BV, Kanungo R, Srinivasan S, Rao RS. Clinico-bacteriological study of neonatal conjunctivitis. Indian J Pediatr 1990;57:527–531. [PubMed: 2286405]
7. Holbrook KF, Nottebart VF, Hameed SR, Platt R. Automated postdis-charge surveillance for postpartum and neonatal nosocomial infections. Am J Med 1991;91(suppl 3B):125S–30S. [PubMed: 1928153]
8. Taylor, D. External eye disease.. In: Taylor, D., editor. Paediatric Ophthalmology. Blackwell; Malden, MA: 1997. p. 185-186.
9. Tan A, Rubin PAD, Sutula FC, Remulla HD. Congenital nasolacrimal duct obstruction. Int Ophthalmol Clin 2001;41:57–69. [PubMed: 11698738]
10. King S, Devi SP, Mindorff C, Patrick ML, Gold R, Ford-Jones L. Nosocomial *Pseudomonas aeruginosa* conjunctivitis in a pediatric hospital. Infect Control Hosp Epidemiol 1988;9:77–80. [PubMed: 3125244]
11. Raskind CH, Sabo BE, Callan DA, Farrel PA, Dembry ML, Gallagher PG. Conjunctival colonization of infants hospitalized in a neonatal intensive care unit: a longitudinal analysis. Infect Control Hosp Epidemiol 2004;25:216–220. [PubMed: 15061413]
12. Rao K, Ramji S, Thirupuram S, Prakash K. Clinical and bacteriological study of normal and inflamed neonatal conjunctivae. Indian Pediatr 1992;29:161–165. [PubMed: 1592495]
13. King RA. Common ocular problems in children: conjunctivitis and tear duct obstructions. Pediatrician 1990;17:142–151. [PubMed: 2194179]

TABLE 1

Demographics of the Study Population

Variable	Mean or No. of Admissions
Gender	
Female	1295 (44)*
Male	1640 (56)
Year of study	
1	1466 (50)
2	1,469 (50)
Study site	
NICU 1	1,694 (58)
NICU 2	1,241 (42)
Birth wt (g); range	2,420; 375–5740
Ventilator (d); range	2.9; 0–361
NC-CPAP (d); range	4.3; 0–153
Length of stay (d); range	17.6; 1–361

* Numbers in parentheses, percent.

TABLE 2

Organisms Causing Health Care-Acquired Conjunctivitis

Organism	Total No. of Isolates*
Coagulase-negative *Staphylococcus*	38 (25)†
Staphylococsus aureus	29 (19)
Klebsiella spp.	16 (10)
Pseudomonas aeruginosa	13 (8)
Enterococcus spp.	13 (8)
Escherichia coli	12 (8)
Serratia marcescens	12 (8)
Enterobacter spp.	10 (6)
Streptococcus spp.	9 (6)
Other Gram-negative bacilli	11 (7)
Diphtheroids	3 (2)
Yeast	4 (3)
Culture not obtained	33 (21)
Total	203 (131)*

* Includes 44 cases with >1 organism isolated.

† Numbers in parentheses, percent of cases.

TABLE 3

Predictors of Health Care-Acquired Conjunctivitis In 2 Study NICUs, Logistic Regression Model

Variable	Odds Ratio	*P*
Birth wt (g)		
<1000	7.9 (4.6,13.4)*	<0.001
1001−1500	6.4 (3.7,11)	<0.001
1501−2500	1.9 (1.1,3.4)	0.03
>2500	1.0	Referent
Year of Study 2	1.5 (1.0,2.1)	0.03
>Mean (4.3) NC-CPAP days	2.1 (1.4,3.1)	<0.001
>Mean (2.9) ventilator days	2.0 (1.4,2.9)	<0.001

* Numbers in parentheses, 95% CI.

TABLE 4

Logistic Regression Analysis of NICU 1, With Eye Examination Variable Included

Variable	Odds Ratio	*P*
Birth wt (g)		
<1000	17 (7.7, 37.5)*	<0.001
1001−1500	5 (2.0, 12.8)	0.01
1501−2500	1.8 (0.7, 4.7)	0.2
>2500	1.0	Referent
>Mean (4.3) NC-CPAP days	5.3 (2.9, 9.4)	<0.001
>Mean (2.9) ventilator days	2.0 (1.1, 3.4)	0.014
Prior eye examinations†	3.7 (1.8, 7.4)	<0.001

*Numbers in parentheses, 95% CI.

†All eye examinations performed during NICU hospitalization in uninfected infants versus eye examinations performed before conjunctivitis in case infants.