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Trends in Infantile Endogenous Endophthalmitis Hospitalizations in the United States:

An Analysis from 2007 through 2014 Using the National Inpatient Sample

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Abstract

Purpose: To determine the annual change in incidence of neonatal and infantile endogenous endophthalmitis in the United States between 2007 and 2014 and identify associated risk factors for development of endophthalmitis and mortality.

Design: Retrospective cross-sectional study.

Participants: Neonates (<28 days; n = 1650) hospitalized for endogenous endophthalmitis between 2003 and 2014 and infants (age range, 28 dayse–1 year; n = 1850) hospitalized between 2007 and 2014 across United States community hospitals were analyzed.

Methods: The Nationwide Inpatient Sample database was queried to identify neonates hospitalized for endogenous endophthalmitis between 2003 and 2014 and infants hospitalized between 2007 and 2014 across the United States. National and regional incidence of neonatal and infantile endogenous endophthalmitis and comorbidities as well as risk factors in the development of the disease and predictive factors for mortality from the years 2007 through 2014 were calculated.

Main Outcomes and Measures: National incidence, regional incidence, and risk factors for development of neonatal and infantile endogenous endophthalmitis.

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Results: The rate of decline in incidence of neonatal endogenous endophthalmitis was 4% from 2003 through 2014. The rate of decline in the infantile population was 7% from 2007 through 2014. In 2007, an estimated 291 total cases of infantile endophthalmitis were identified, in comparison with 140 cases in 2014. Comorbidities prevalent in the endophthalmitis population included prematurity, respiratory disorders, perinatal infections, and retinopathy of prematurity (ROP). Significant positive predictors for the development of endogenous endophthalmitis based on multivariate logistic regression were perinatal infections, candidemia, bacteremia, very low birth weight, prematurity, respiratory disorders, and ROP. Descriptive analyses showed that the in-hospital mortality rate for patients identified with endophthalmitis was 1.55% in comparison with infants without endophthalmitis.

Conclusions: The incidence of endogenous endophthalmitis declined in both the neonatal and infantile population from 2007 through 2014. Odds of endogenous endophthalmitis were higher for premature and low-birthweight infants and those identified with perinatal infections, candidemia, bacteremia, respiratory disorders, or ROP. These findings are consistent with the decline observed in pediatric infectious disease-related hospitalizations in general.

Endogenous endophthalmitis is a severe and potentially blinding emergency that requires prompt management. It occurs when hematogenous spread of micro-organisms occurs across the blood–ocular barrier, leading to infection of intraocular tissues. Most endophthalmitis cases are exogenous, in which the infection results from direct inoculation of micro-organisms through ocular surgeries, trauma, or contiguous spread from adjacent tissues. Endogenous endophthalmitis is uncommon, accounting for only 2% to 8% of all endophthalmitis cases.[1–5] It can occur at any age without a predilection for gender, although in the neonatal and infantile population, an overwhelming majority of cases are endogenous.[6–9] In this population, endogenous endophthalmitis is relatively rare and seen in patients susceptible to risk of infection, including those born prematurely, with low birthweight (<1500 g), with inborn errors of metabolism, and having had an extended hospital stay. Premature neonates and infants are likely to have underdeveloped immune systems and are more prone to respiratory or systemic instability developing.

Endogenous sources can be acquired through maternal vertical transmission in the perinatal period or through community or nosocomial sources, including intravascular devices, contaminated feedings, contaminated respiratory devices, and caregivers. Multiple reports have isolated *Candida* species as the causative organism, particularly in premature and very low-birthweight neonates admitted to the intensive care unit.[6–13] Only a few cases of bacterial and viral isolates have been reported, in which the most prevalent included *Pseudomonas aeruginosa*,[9,14–18] *Escherichia coli*,[19–21] group B *Streptococci*,[22] *Klebsiella pneumonia*,[23] *Staphylococcus aureus*,[14] and herpes simplex virus.[9]

Studies on infantile endogenous endophthalmitis are limited and often restricted to case reports and case series at single academic institutions. The current report represents a nationwide study of neonatal and infantile endogenous endophthalmitis-related hospital admissions in the United States over a 12-year period (2003–2014). It aimed to investigate national and regional trends in incidence of endophthalmitis-related hospitalizations, compare infectious and noninfectious risk factors in the development of endogenous

endophthalmitis to a reference population without the disease, and identify predictive factors for in-hospital mortality.

Methods

Data Source and Study Population

The Nationwide Inpatient Sample (NIS) was queried for the years 2007 through 2014 to identify neonates (<28 days) and infants (<1 year) admitted with a diagnosis of endogenous endophthalmitis. The NIS is part of a set of databases developed for the Healthcare Cost and Utilization Project (HCUP) and is sponsored by the Agency for Healthcare Research and Quality. The NIS is the largest publicly available all-payer inpatient database in the United States containing discharge-level data drawn from all states participating in HCUP and includes more than 97% of the United States population. The database includes clinical and nonclinical information on all patients regardless of payer from hospital discharge records. The database sampling strata are based on hospital characteristics, which include hospital region, urban or rural location, teaching status, bed-size category, and hospital ownership. The data can be weighted based on the NIS sampling frame to create estimates that approximate a nationally representative sample. The sampling frame changes annually; thus, the number of states contributing to the NIS varies from year to year. Beginning with the 2012 data year, the NIS approximated a 20% stratified sample of all discharges from United States community hospitals, excluding rehabilitation and long-term acute care hospitals. To improve national estimates, the database was redesigned to include a 20% stratified sample of discharges from all hospitals in the HCUP. The institutional review board at West Virginia University granted this study exempt status because all data are publicly available and do not include patient identifiers. This study was conducted in adherence to the tenets of the Declaration of Helsinki and United States federal and state laws, including the Health Insurance Portability and Accountability Act.

Study Design

We conducted a retrospective longitudinal study using the NIS database from 2007 through 2014 in the neonatal (<28 days) and infantile (<1 year) population. The NIS provides up to 30 diagnoses and 15 procedures per hospital record, which are coded using the standard International Classification of Diseases, Ninth Edition, Clinical Modification, codes. In the HCUP database, the first listed diagnosis is the principal diagnosis established to be chiefly responsible for admission of the patient to the hospital. The database was queried for neonates and infants with a diagnosis of endophthalmitis (International Classification of Diseases, Ninth Edition, Clinical Modification, code 360.0). Descriptive statistics were calculated for all relevant characteristics, including gender, race, age in days, hospital length of stay, total charges during the inpatient stay, primary expected payer, patient disposition, hospital teaching status, and hospital ownership, and compared with a reference population without the diagnosis of endogenous endophthalmitis. The median age in days, length of stay in days, and charge per hospitalization were reported during the study period. The charges reported in this study represent the amount hospitals billed for the services and do not reflect how much hospital services actually cost, the specific amounts that hospitals received in payment, or the costs incurred to the patients. The database was queried for the

following suspected infectious and noninfectious risk factors associated with the development of endogenous endophthalmitis: sepsis, fungemia, candidemia, bacteremia, viremia, cytomegalic viremia, perinatal infections, retinopathy of prematurity (ROP), birth weight less than 1500 g, prematurity, birth trauma, intrauterine hypoxia and birth asphyxia, necrotizing enterocolitis, respiratory disorders, hemolytic disease of the newborn, respiratory disorders, having undergone retinal laser photocoagulation, fetal hemorrhage, intraventricular hemorrhage, and having received blood transfusions. The variables considered for inclusion were based on previous studies and known clinical correlation.

Outcome Measures

The primary outcome measure was the incidence of the total number of cases of endogenous endophthalmitis in neonates and infants per year throughout the study period. Regional incidence analysis, including the Northeast, Midwest, South, and West regions of the United States, was also conducted over the study period. The incidence rates of endophthalmitis in neonates were weighted according to the total number of live births and, in infants, were weighted according to the total population younger than 1 year over the study period using population data from the United States Census Bureau. Secondary outcome measures included (1) associations of infectious and noninfectious risk factors in the development of endogenous endophthalmitis and (2) associations of these factors with risk of in-hospital mortality. Mortality data after discharge were not included in the analyses.

Statistical Analysis

Descriptive statistics were calculated for all relevant characteristics and are presented as frequencies with percentages for categorical variables and as the median or mean with standard deviation for continuous variables. Comparisons between groups were made using the Student *t* test for continuous variables and the chi-square test for categorical variables. All variables and observances in the dataset were weighted to calculate projected national and regional estimates for each hospital admission using discharge weights. Linear regression was used to estimate the changes in the annual incidence of endophthalmitis in both the neonate and infant population, as derived from HCUP national estimates and United States Census Bureau population data. Regional population estimates were produced by linking the NIS Hospital Weights File and Core Data File and applying the appropriate hospital weighted data. Multivariate logistic regression analyses were used to estimate risk (odds ratios [ORs]) of endophthalmitis development and in-hospital mortality. All *P* values less than 0.05 were considered statistically significant. Statistical analyses were performed using SAS software version 9.4 (SAS Institute, Inc, Cary NC).

Results

Demographics and Baseline Characteristics

Demographics and baseline characteristics are described in Table 1. From 2003 through 2014, an estimated 1650 neonates (<28 days) were identified with endogenous endophthalmitis in the United States. From 2007 through 2014, an estimated 1850 infants (<1 year) were identified with endogenous endophthalmitis. The mean age for hospitalized infants with endogenous endophthalmitis was 30 days. A plurality of the population was

white (37.29%), followed by Hispanic (24.01%), black (18.27%), Asian (3.96%), and Native American (1.42%). The median length of hospital stay was longer in infants diagnosed with endophthalmitis (9 days vs. 2 days; $P < 0.0001$). The median total charges incurred during a hospital admission was a magnitude higher for those diagnosed with endophthalmitis ($38 967 vs. $3212; $P < 0.0001$).

In the regional analysis, the highest frequency of admissions was from the South (36%), followed by the Midwest (26%), West (26%), and Northeast (16%). Most patients were insured publicly through Medicaid (53.52% vs. 44.90% without endophthalmitis; $P < 0.001$). The most common discharge disposition was home or self-care (82.38% vs. 94.29% without endophthalmitis), followed by home health care (8.32%) and transfer to another facility (4.75%). Most admissions were in not-for-profit (72.99% vs. 66.34%) teaching (71.75% vs. 52.27%) hospitals. The in-hospital mortality rate in infants diagnosed with endogenous endophthalmitis was significantly higher than in those without endophthalmitis (1.55% vs. 0.41%; $P < 0.001$).

National and Regional Trends in the Incidence of Endogenous Endophthalmitis-Related Hospitalizations

The total incidence of neonatal endogenous endophthalmitis related hospitalizations in the United States was 3.64 per 100 000 population between 2003 and 2014, and the total incidence of infantile endogenous endophthalmitis-related hospitalizations was 5.78 per 100 000 population between 2007 and 2014. In both the neonatal and infantile population, an overall declining trend during the study period was found. The average rate of decline in the incidence of neonatal endogenous endophthalmitis was 4% ($P = 0.0025$) from 2003 through 2014, compared with an average 7% ($P = 0.0027$) decline in the infantile population from 2007 through 2014. In the neonatal population, the incidence peaked in 2005 (5.47 per 100 000 population), after which it declined, with the lowest incidence occurring in 2014 (2.44 per 100 000 population; Fig 1). In the infantile population, the incidence was high from more recent years 2007 through 2009 (approximately 7–7.5 per 100 000 population), with the lowest incidence observed in 2014 (3.54 per 100 000 population; Fig 2). The regional analysis showed an overall decreasing trend from 2007 through 2014 in all 4 regions for the infantile population (Fig 3). In 2011, an increase in the incidence rate occurred in the Northeast (10.83 per 100 000), South (9.89 per 100 000), and Midwest (8.0 per 100 000), after which a sharp decline occurred. Similar incidence rates were seen across all 4 regions from 2011 through 2012, with the lowest rates seen in the West and Northeast regions in 2014.

Prevalence of Infectious and Noninfectious Causes

The prevalence of comorbid conditions in infants with and without endogenous endophthalmitis is shown in Table 2. In the infantile population identified with endogenous endophthalmitis, the most common infectious cause was fungemia (1.51% vs. 0.03%; $P < 0.0001$), followed by bacteremia (1.31% vs. 0.15%; $P < 0.0001$), candidemia (0.81% vs. 0.02%; $P < 0.0001$), cytomegalic disease (0.23% vs. 0.01%; $P < 0.0001$), and viremia (0.23 vs. 0.013; $P = 0.99$). Perinatal infections were significantly more common in infants with endophthalmitis compared with those without (26.29% vs. 2.81%; $P < 0.0001$). The most

common systemic risk factor was prematurity (born <37 weeks' gestation) in infants with endophthalmitis (36.09% vs. 8.72%; $P < 0.0001$), followed by respiratory disorders (32.33% vs. 8.39%; $P < 0.0001$), ROP (7.76 vs. 0.45%; $P < 0.0001$), intraventricular hemorrhage (4.75% vs. 0.41%; $P < 0.0001$), birth trauma (2.04% vs. 2.65%; $P = 0.069$), necrotizing enterocolitis (1.53% vs. 0.16%; $P < 0.0001$), and intrauterine hypoxia and birth asphyxia (0.67% vs. 0.26%; $P < 0.0002$). A limited number of patients either with or without endophthalmitis were identified with fetal hemorrhage, hemolytic disease of the newborn, or blood transfusion procedures.

Risk Factors for Infantile Endogenous Endophthalmitis Developing

Multivariate logistic regression models from 2007 through 2014 were used to examine the association between infectious and noninfectious risk factors in the development of infantile endogenous endophthalmitis (Table 3). Variable selection for the multivariate logistic regression model was based on known clinical correlations and previous studies. Regression analysis identified perinatal infections (OR, 5.04; 95% confidence interval [CI], 4.47–5.68; $P < 0.0001$), candidemia (OR, 9.08; 95% CI, 5.45–14.14; $P < 0.0001$), bacteremia (OR, 2.71; 95% CI, 1.83–3.85; $P < 0.0001$), prematurity (OR, 2.40; 95% CI, 2.14–2.68; $P < 0.0001$), respiratory disorders (OR, 1.68; 95% CI, 1.50–1.89; $P < 0.0001$), ROP (OR, 2.51; 95% CI, 2.08–3.01; $P < 0.0001$), and very low birthweight (<1500 g; OR, 1.39; 95% CI, 1.14–1.68; $P < 0.0001$) as positive predictors for endogenous endophthalmitis. Gender, fetal hemorrhage, intraventricular hemorrhage, necrotizing enterocolitis, birth trauma, hypoxia, and hemolytic disease of the newborn were not significant predictors for development of disease.

Risk of Mortality in Hospitalized Infants with or without Endophthalmitis

Risk of mortality in hospitalized infants with or without endophthalmitis was analyzed using multivariate logistic regression analysis (Table 4). Very low-birthweight infants weighing less than 1500 g showed a 70-fold increase in mortality (OR, 77.51; 95% CI, 76.51–78.53; $P < 0.05$). Infants admitted to a teaching hospital ($P < 0.05$) or diagnosed with viremia ($P < 0.05$), bacteremia ($P > 0.05$), cytomegalic disease ($P < 0.05$), and fungemia ($P < 0.05$) showed an increased likelihood of mortality. A decreased likelihood for mortality was seen for female gender ($P < 0.05$), white race ($P < 0.05$), and those identified with endophthalmitis ($P < 0.05$).

Discussion

In this analysis using the publicly available NIS database, a large nationally representative database of inpatient hospitalizations in the United States, we demonstrated declining trends in the neonatal and infantile endogenous endophthalmitis hospitalizations in the United States from 2007 through 2014 and characterized risk factors for endophthalmitis development. Our nationally representative sample extends the breadth of currently existing literature on pediatric endogenous endophthalmitis hospitalizations. Studies are limited and often restricted to case reports or case series at single academic institutions, and the population demographics are not representative of the United States population at large. Within the last decade, Moshfeghi et al[6] published a nationwide study using the NIS

database describing endogenous endophthalmitis trends from 1998 through 2006 and validated the commonly held belief that candidemia, bacteremia, ROP, and low birthweight were significant risk factors for the development of endophthalmitis.

We sought to extend this trend analysis in the neonatal and infantile population across all 4 United States regions: the West, South, Midwest, and Northeast. We replicated the methodology published by Moshfeghi et al and were able to reproduce very similar neonatal endophthalmitis case numbers and incidence rates from 2003 through 2006, which are included in Figure 1A. Although Moshfeghi et al reported a decline in endophthalmitis incidence at a rate of 6% per year ($P = 0.0113$) from 1998 to 2006, we found that the average rate of decline was 4% per year ($P = 0.0025$) in the neonatal population from 2003 through 2014 and 7% ($P = 0.0027$) in the infantile population from 2007 through 2014. The decline in endophthalmitis cases mirrors the overall downward trend in ID pediatric hospitalizations, particularly in children younger than 1 year.[24] A significant number of neonatal hospitalizations are attributed to IDs,[24–26] causing widespread morbidity and mortality. The federal government has identified the public health burden of IDs among infants and has aimed to reduce the number of ID-related hospitalizations in this population as one of the objectives for Healthy People 2020.[27]

Goto et al[24] examined the change in epidemiologic characteristics of pediatric ID hospitalizations in United States children from 2000 through 2012 using the HCUP's Kids' Inpatient Database, a national database of United States pediatric hospitalizations, and found a statistically significant overall decline in ID hospitalizations. They identified infants whose records contained an International Classification of Diseases, Ninth Edition, Clinical Modification, code for an ID diagnosis in the primary diagnosis field, which included perinatal period-specific codes and ID-specific subgroups ranging from viral central nervous system infections to respiratory infections. In 2012, the most common ID diagnoses in infants were lower respiratory infections (including pneumonia and bronchitis, 61%), followed by urinary tract infections (9%) and septicemia (8%). The authors reported an overall decreased hospitalization rate from 91 to 75 per 10 000 United States children (16.5% decease; $P < 0.001$), which was largely the result of the decrease in the national rate among children younger than 1 year (30.3% decrease; $P < 0.001$) from 2000 through 2012. This declining trend could be attributed to better surveillance, preventative measures, and treatments as well as medical and technological advancements within the 7-year study period.

The most frequently reported infectious comorbidities in our study were respiratory disorders and perinatal infections, with fungal pathogens as the most common infectious cause. *Candida* species have been characterized as the primary responsible organisms in multiple case series and reports in the United States,[7,9,28–31] whereas gram-negative bacterial isolates, especially *P. aeruginosa*, have been reported more frequently in India,[14,17] Germany,[15,32] and Portugal.[33] The most commonly reported systemic comorbidities in our study were prematurity (<27 weeks' gestation), very low birthweight (<1500 g), and ROP. Premature, low-birthweight, and neonatal intensive care unit infants in particular are susceptible to *Candida* endophthalmitis because of the deficient host defense mechanisms and exposure to pathogens in a hospital setting. Using multivariate regression analysis, we

found that prematurity, low birthweight, perinatal infections, candidemia, bacteremia, and respiratory disorders were significant predictors for disease development. Except for prematurity, all of these same variables were significant predictors reported by Moshfeghi et al; female gender did show a reduced likelihood of endophthalmitis development, whereas our gender analysis did not show statistical significance. We also found a 2-fold increased the likelihood of endophthalmitis development in infants diagnosed with ROP ($P < 0.0001$). A plausible explanation could be that these infants have increased vascular permeability because of upregulated vascular endothelial growth factor, allowing for dissemination of septic emboli to the eye.[9] Stage 3 or worse ROP is often seen in susceptible premature, low-birthweight infants, especially those weighing less than 1000 g.[34] Previous studies have suggested a strong association between ROP development and fungal sepsis, especially *Candida* pathogens. Ophthalmic evaluations are indicated in this high-risk population with *Candida* species infections, because early detection may improve outcomes.

Pediatric ID-related hospitalizations are associated with significant healthcare burdens and expenditures in the United States. Goto et al[24] reported that the median direct cost for ID hospitalization increased from $3452 in 2003 to $3784 in 2012 ($P = 0.007$), with the nationwide direct cost of $4.4 billion in 2012. In our study, we found that the median direct costs among infants diagnosed with endophthalmitis ($38 967) were an order of magnitude higher than those for infants without endophthalmitis ($3212). This could be attributed to the longer hospital stay in infants with endophthalmitis (mean, 30 days) compared with infants without endophthalmitis (mean, 7 days). This population likely may have other concomitant comorbidities requiring further treatment interventions and, as a result, higher resources. Infants with endophthalmitis were less likely to be discharged home compared with those without (82.38% vs. 94.29%; $P < 0.0001$), necessitating transfer to another facility, such as a teaching hospital, or to home with home health care, further adding to hospital charges. Infants with endophthalmitis were more likely to be admitted to a teaching hospital (71.75% vs. 52.27% without endophthalmitis; $P < 0.0001$), where medically complex cases are usually referred.

The strengths of this study include a large sample size and nationwide estimates, representative of the United States infantile population. Because exogenous endophthalmitis is extremely uncommon in the infantile population, whether acquired by trauma, invasive organisms on the ocular surface, or postsurgical interventions, we concluded that the overwhelming majority of cases were endogenous. We also recognize that this study has several other limitations. With any study using administrative data, potential for misdiagnoses exists. However, with the large sample size, the potential misdiagnoses should not have varied during the study period and may not have a substantial impact on our analysis. The NIS contains deidentified discharge-level records and not patient-level records, and multiple-hospital admissions could not be identified. Patient outcomes beyond hospital discharge are not available.

Endophthalmitis-related hospitalizations along with general pediatric ID-related hospitalizations have been on the decline in recent years. We have shown that vulnerable premature, low-birthweight infants are most likely to demonstrate endophthalmitis resulting

from vertical or horizontal transmission in the healthcare setting, and ophthalmic screenings are warranted in high-risk infants.

Abbreviations and Acronyms:

CI	confidence interval
HCUP	Healthcare Cost and Utilization Project
ID	infectious disease
NIS	Nationwide Inpatient Sample
OR	odds ratio
ROP	retinopathy of prematurity

References

1. Connell PP, O'Neill EC, Fabinyi D, et al. Endogenous endophthalmitis: 10-year experience at a tertiary referral centre. Eye (Lond). 2011;25:66e72. [PubMed: 20966972]
2. Okada AA, Johnson RP, Wiles WC, et al. Endogenous bacterial endophthalmitis. Report of a ten-year retrospective study. Ophthalmology. 1994;101:832e838. [PubMed: 8190467]
3. Jackson TL, Eykyn SJ, Graham EM, Stanford MR. Endogenous bacterial endophthalmitis: a 17-year prospective series and review of 267 reported cases. Surv Ophthalmol. 2003;48: 403e423. [PubMed: 12850229]
4. Chee SP, Jap A. Endogenous endophthalmitis. Curr Opin Ophthalmol. 2001;12(6):464e470. [PubMed: 11734687]
5. Schiedler V, Scott IU, Flynn HW, et al. Culture-proven endogenous endophthalmitis: clinical features and visual acuity outcomes. Am J Ophthalmol. 2004;137:725e731. [PubMed: 15059712]
6. Moshfeghi AA, Charalel RA, Hernandez-Boussard T, et al. Declining incidence of neonatal endophthalmitis in the United States. Am J Ophthalmol. 2011;151:59e65 e1. [PubMed: 20970776]
7. Baley JE, Ellis FJ. Neonatal candidiasis: ophthalmologic infection. Semin Perinatol. 2003;27:401e405. [PubMed: 14626504]
8. Noyola DE, Fernanadez M, Moylett EH, Baker CJ. Ophthalmologic, visceral, and cardiac involvement in neonates with candidemia. Clin Infect Dis. 2001;32:1018e1023. [PubMed: 11264029]
9. Aziz HA, Berrocal AM, Sisk RA, et al. Intraocular infections in the neonatal intensive care unit. Clin Ophthalmol. 2012;6: 733e737. [PubMed: 22654500]
10. Donahue SP, Hein E, Sinatra RB. Ocular involvement in children with candidemia. Am J Ophthalmol. 2003;135: 886e887. [PubMed: 12788131]
11. Palmer EA. Endogenous Candida endophthalmitis in infants. Am J Ophthalmol. 1980;89:388e395. [PubMed: 6966132]
12. Stern JH, Calvano C, Simon JW. Recurrent endogenous candidal endophthalmitis in a premature infant. J AAPOS. 2001;5: 50e51. [PubMed: 11182674]
13. Shah GK, Vander J, Eagle RC. Intralenticular Candida species abscess in a premature infant. Am J Ophthalmol. 2000;129: 390e391. [PubMed: 10704563]
14. Basu S, Kumar A, Kapoor K, et al. Neonatal endogenous endophthalmitis: a report of six cases. Pediatrics. 2013;131: e1292ee1297. [PubMed: 23478867]
15. Lohrer R, Belohradsky BH. Bacterial endophthalmitis in neonates. Eur J Pediatr. 1987;146:354e359. [PubMed: 3308466]

16. Mithal K, Mathai A, Pathengy A, et al. Endophthalmitis following intravitreal anti-VEGF injections in ambulatory surgical centre facility: incidence, management and outcome. Br J Ophthalmol. 2013;97:1609e1612.
17. Jalali S, Pehere N, Rani PK, et al. Treatment outcomes and clinicomicrobiological characteristics of a protocol-based approach for neonatal endogenous endophthalmitis. Eur J Ophthalmol. 2014;24:424e436. [PubMed: 24338573]
18. Sanchez-Tocino H, Sanabria MR, Catala-Mora J, et al. Bilateral endogenous endophthalmitis due to pseudomonas aeruginosa in a neonate. Retin Cases Brief Rep. 2008;2: 190e192. [PubMed: 25390082]
19. Wu Z, Uzcategui N, Chung M, et al. Group B streptococcal endogenous endophthalmitis in a neonate. Retina. 2006;26: 472e473. [PubMed: 16603970]
20. Wu Z, Huang J, Huynh S, Sadda S. Bilateral endogenous endophthalmitis secondary to group B streptococcal sepsis. Chin Med J (Engl). 2014;127:1999. [PubMed: 24824276]
21. Friedlander SM, Raphaelian PV, Granet DB, Goldbaum MH. Bilateral endogenous Escherichia coli endophthalmitis in a neonate with meningitis. Retina. 1996;16:341e342. [PubMed: 8865397]
22. Clavell C, Athwal L, Zarbin MA, et al. Pediatric infectious endophthalmitis: a case series. J Pediatr Ophthalmol Strabismus. 2018;55:69e70. [PubMed: 29378081]
23. Li G, Little JM, Santanna G, Polomeno RC. Presumed endogenous Klebsiella pneumonia endophthalmitis in a premature infant. J AAPOS. 2004;8:398e400. [PubMed: 15314607]
24. Goto T, Tsugawa Y, Mansbach JM, et al. Trends in infectious disease hospitalizations in US children, 2000 to 2012. Pediatr Infect Dis J. 2016;35:e158ee163. [PubMed: 26967815]
25. Yorita KL, Holman RC, Sejvar JJ, et al. Infectious disease hospitalizations among infants in the United States. Pediatrics. 2008;121:244e252. [PubMed: 18245414]
26. Christensen KL, Holman RC, Steiner CA, et al. Infectious disease hospitalizations in the United States. Clin Infect Dis. 2009;49:1025e1035. [PubMed: 19708796]
27. National Center for Health Statistics, Centers for Disease Control and Prevention Healthy People 2020 midcourse review. Hyattsville, MD: National Center for Health Statistics, Centers for Disease Control and Prevention, United States Department of Health and Human Services; 2016.
28. Khan S, Athwal L, Zarbin M, Bhagat N. Pediatric infectious endophthalmitis: a review. J Pediatr Ophthalmol Strabismus. 2014;51:140e153. [PubMed: 24877526]
29. Benjamin DK Jr, Poole C, Steinbach WJ, et al. Neonatal candidemia and end-organ damage: a critical appraisal of the literature using meta-analytic techniques. Pediatrics. 2003;112:634e640. [PubMed: 12949295]
30. Dozier CC, Tarantola RM, Jiramongkolchai K, Donahue SP. Fungal eye disease at a tertiary care center: the utility of routine inpatient consultation. Ophthalmology. 2011;118: 1671e1676. [PubMed: 21550121]
31. Zaoutis TE, Heydon K, Localio R, et al. Outcomes attributable to neonatal candidiasis. Clin Infect Dis. 2007;44:1187e1193. [PubMed: 17407037]
32. Ness T, Pelz K, Hansen LL. Endogenous endophthalmitis: microorganisms, disposition and prognosis. Acta Ophthalmol Scand. 2007;85:852e856. [PubMed: 17725616]
33. Figueirido S, Joao A, Mateus M, et al. Endogenous endophthalmitis caused by Pseudomonas aeruginosa in a preterm infant: a case report. Cases J. 2009;2:9304. [PubMed: 20062628]
34. Mittal M, Dhanireddy R, Higgins RD. Candida sepsis and association with retinopathy of prematurity. Pediatrics. 1998;101:654e657. [PubMed: 9521951]

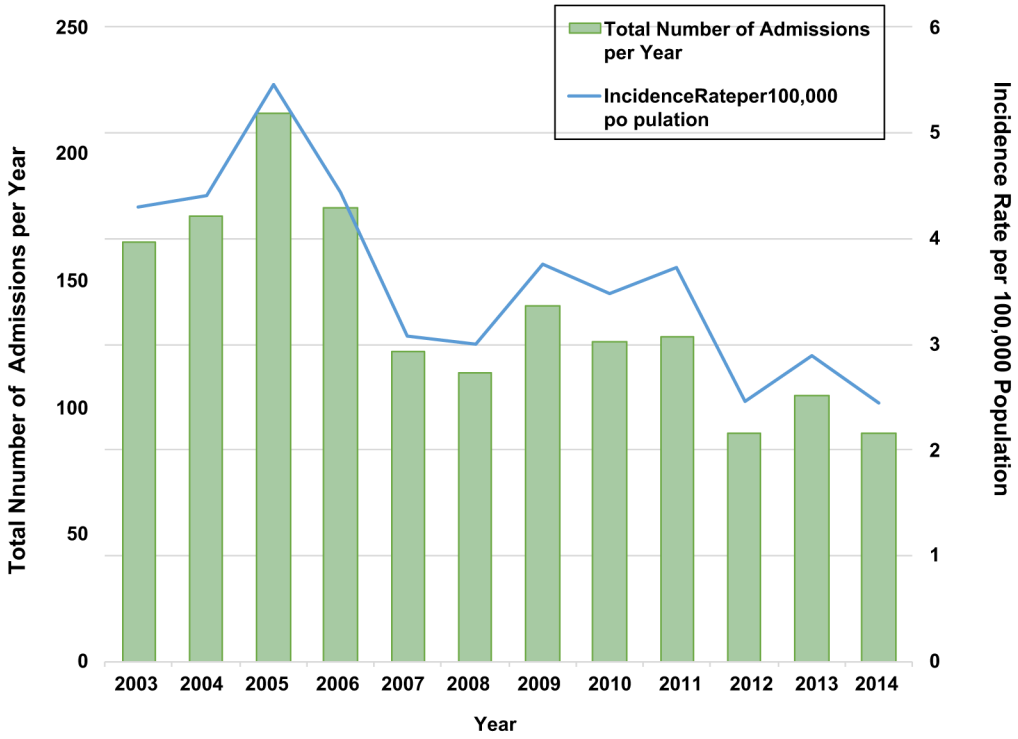

Figure 1.

Graph showing the incidence of neonatal endogenous endophthalmitis-related hospitalizations in the United States, 2003 through 2014.

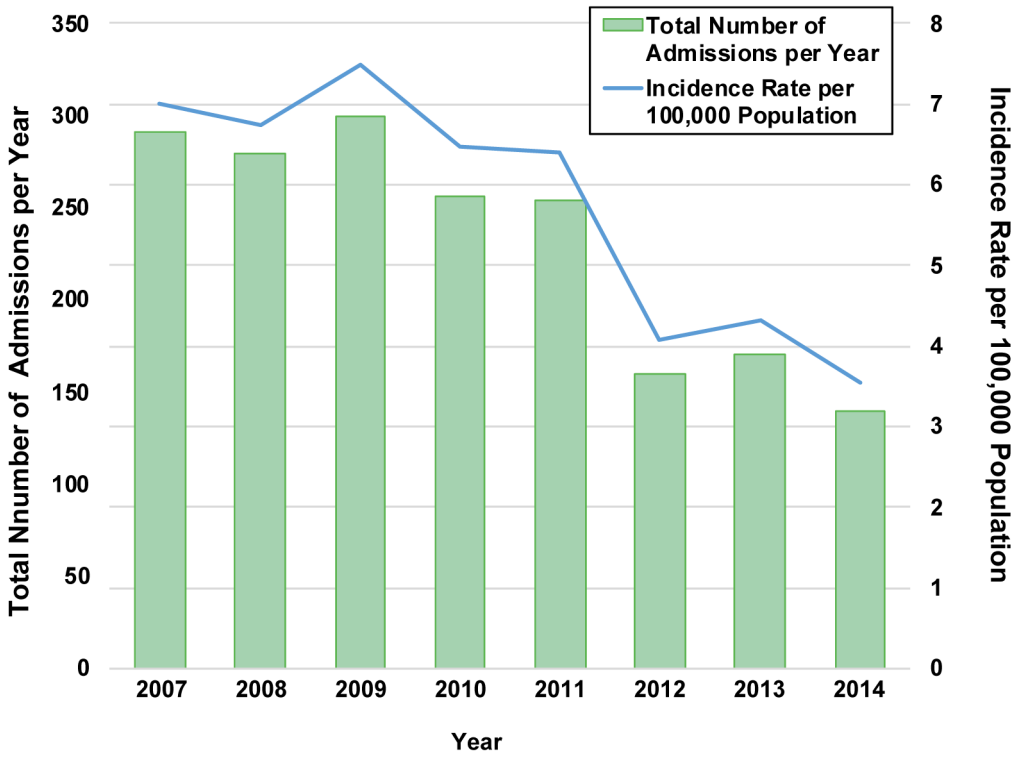

Figure 2.

Graph showing the incidence of infantile endogenous endophthalmitis-related hospitalizations in the United States, 2007 through 2014.

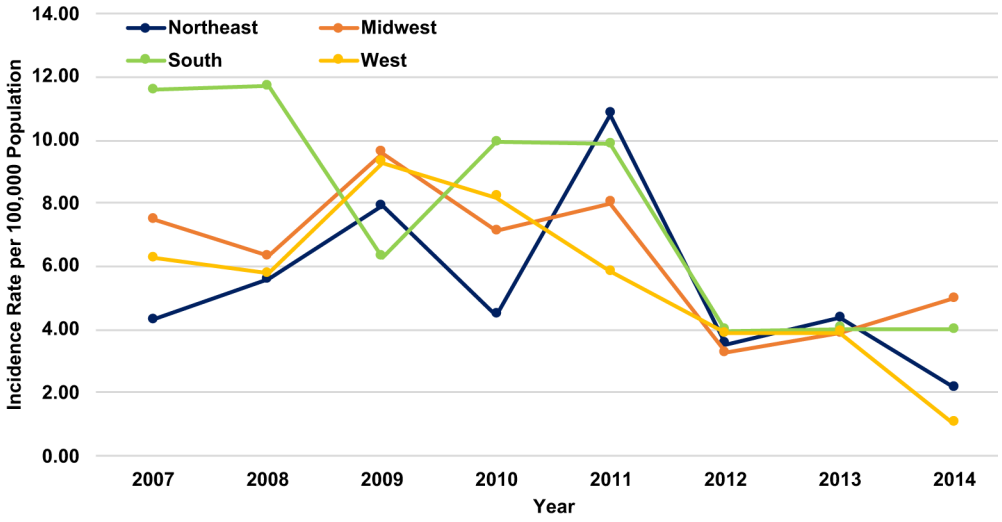

Figure 3.

Line graph showing a regional comparison of the incidence rate of infantile endogenous endophthalmitis.

Table 1.

Characteristics of Neonates and Infants with (n = 1850) and without Endogenous Endophthalmitis, 2007 through 2014

	Total Population	Infants with Endophthalmitis (n = 1850)	Infants without Endophthalmitis (n = 31.69 Million)	*P* Value
Baseline characteristics				
Female gender	45.30			
Race				
White	37.29			
Black	18.27			
Hispanic	24.01			
Asian	3.96			
Native American	1.42			
Primary expected payer				
Medicaid	53.52			
Private insurance	41.19			
Self-pay	3.49			
Disposition of patient				
Home health care	8.32			
Routine home or self-care	82.38			
Transfer to short-term hospital	0.87			
Transfer to another facility	4.75			
Inpatients with routine discharge		82.38	94.29	<0.0001
In-hospital mortality		1.55	0.41	<0.0001
Teaching hospital		71.75	52.27	<0.0001
Female gender		45.30	48.29	0.0046
Medicaid beneficiary		53.52	44.90	<0.0001
White race		37.29	44.29	<0.0001
Nonprofit hospital		72.99	66.34	<0.0001
Age (days)				
Mean (SD)		30.37 (68.53)	7.20 (37.60)	
Median		1	0	<0.0001
Median length of stay (days)		9	2	<0.0001

	Total Population	Infants with Endophthalmitis (n = 1850)	Infants without Endophthalmitis (n = 31.69 Million)	P Value
Total median charges ($)		38 967	3212	<0.0001

SD=standard deviation

Data are percents unless otherwise indicated

Table 2.

Prevalence (%) of Comorbid Conditions in Infants with and without Endogenous Endophthalmitis

	Infants with Endophthalmitis (n = 1850)	Infants without Endophthalmitis (n = 31.69 Million)	*P* Value
Retinopathy of prematurity	7.76	0.45	<0.0001
Respiratory disorders	32.33	8.39	<0.0001
Perinatal infections	26.29	2.81	<0.0001
Fetal hemorrhage	0	0.02	0.9999
Intraventricular hemorrhage	4.75	0.41	<0.0001
Blood transfusion	0	0.00014	0.9999
Necrotizing enterocolitis	1.53	0.16	<0.0001
Hypoxia	0.67	0.26	0.0002
Birth trauma	2.04	2.65	0.0695
Hemolytic disease	0	0.01	0.9999
Prematurity	35.04	8.72	<0.0001
Bacteremia	1.31	0.15	<0.0001
Candidemia	0.81	0.02	<0.0001
Cytomegalic disease	0.23	0.01	<0.0001
Fungemia	1.51	0.03	<0.0001
Viremia	0.23	0.013	0.9999

Table 3.

Predictive Variables of Infantile Endogenous Endophthalmitis Based on Logistic Regression

	Odds Ratio	95% Confidence Interval	*P* Value
Candidemia	9.08	5.45–14.14	<0.0001
Very low birthweight (<1500 g)	1.39	1.14–1.68	0.0009
Prematurity	2.40	2.14–2.68	<0.0001
Female gender	0.93	0.86–1.02	0.1085
Bacteremia	2.71	1.83–3.85	<0.0001
Retinopaty of prematurity	2.51	2.08–3.01	<0.0001
Respiratory disorders	1.68	1.50–1.89	<0.0001
Perinatal infections	5.04	4.47–5.68	<0.0001
Fetal hemorrhage	0.35	0.003–2.36	0.9115
Intraventricular hemorrhage	1.13	0.91–1.40	0.267
Necrotizing enterocolitis	0.81	0.56–1.14	0.2466
Birth trauma	0.75	0.55–0.99	0.0503
Hypoxia	1.26	0.72–2.03	0.3695
Hemolytic disease	1.08	0.83–1.38	0.5337

Table 4.

Risk of Mortality in Hospitalized Infants Based on Logistic Regression

	Odds Ratio	95% Confidence Interval	*P* Value
Viremia	13.987	9.52–19.77	<0.05
Endophthalmitis *	0.535	0.35–0.78	<0.05
Female gender	0.859	0.85–0.87	<0.05
White race	0.932	0.92–0.94	<0.05
Very low birthweight (<1500 g)	77.51	76.51–78.53	<0.05
Teaching status	1.929	1.90–1.96	<0.05
Bacteremia	1.064	0.97–1.17	>0.05
Candidemia	0.495	0.40–0.61	<0.05
Cytomegalic disease	1.382	1.13–1.68	<0.05
Fungemia	6.019	5.07–7.15	<0.05

* An effect modification by birthweight was found. Endophthalmitis was an independent predictor of mortality in infants weighing more than 1500 g (odds ratio, 2.713; 95% confidence interval, 1.598–4.300; $P < 0.05$).