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State-Based Analysis of Necrotizing Enterocolitis Outcomes[1]

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Background. **Necrotizing enterocolitis (NEC) is a devastating disease of the newborn. We hypothesized that patient and institution level factors lead to NEC-related outcome disparities.**

Methods. **We analyzed the California Office of Statewide Health Planning and Development database for the years 1999–2004. We selected NEC-specific ICD-9-CM diagnosis and procedure codes. Mortality rate was the primary outcome measure, and length of stay was used a secondary end-point. We stratified the data by birth weight, gender, race/ethnicity, treatment, median household income, insurance status, admission type (inborn or outborn), and NICU levels.**

Results. **We identified 3328 infants with NEC (incidence of 1 per 1000 live births). Overall mortality within the NEC cohort was 12.5% (13.4 deaths per 100,000 live births). Male or Hispanic neonates were less likely to survive. Socioeconomic factors, including insurance status and parental median household income, were not predictors of mortality. Neonates treated surgically had a greater mortality rate compared with ones treated nonsurgically. PDA was present in 32% of patients with NEC, and these neonates were more likely to undergo gastrointestinal surgery. The odds of NEC-associated mortality in level IIIC units were significantly greater than any other NICU level. Admission type (inborn *versus* outborn) was not associated with increased mortality.**

Conclusions. **Disparities in NEC outcomes are multifactorial with patient- and treatment-specific factors contributing significantly to the unfavorable outcomes. These data suggest that advances in prediction modeling, prevention, and treatment algorithms are needed for clinicians and state health planners to positively impact this costly neonatal condition.**

Key Words: **neonate; mortality; disparity; enterocolitis.**

INTRODUCTION

Due to the rising preterm and low birth weight deliveries [1, 2], and improving infant survival rates [3, 4], the at-risk population for necrotizing enterocolitis (NEC) persists [5, 6]. NEC is among the leading causes of neonatal mortality[7] and the most common reason for emergency gastrointestinal surgery during the neonatal period [8, 9]. Despite decades of NEC research, many unanswered questions remain regarding its pathogenesis [10-13], treatment [14], prevention [15], and epidemiology [16, 17]. Each neonatal NEC-associated hospitalization costs approximately $300,000, and an infant requiring surgical care adds nearly $200,000 to the cost of neonatal care in comparison to other premature infants [18]. Moreover, the initial cost and care is only the tip of the iceberg because survivors are prone to future gastrointestinal and neurodevelopmental morbidities [19–24]. Given the burden NEC poses on the families and institutions caring for these infants, it is vital to determine strategies to improve outcomes associated with this condition.

Prematurity is the most important comorbidity leading to NEC [5, 17, 25]. Infants require intensive care management for prematurity, low birth weight, intrauterine growth retardation, congenital malformations

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(birth defects), sepsis, birth asphyxia, or pulmonary insufficiency. One commonly associated condition with prematurity is patent ductus arteriosus (PDA). Infants with PDAs are at risk for development of NEC [20, 25–28]. Not only the presence of PDA is a risk factor for NEC, but also the medical treatment of PDA with indomethacin is associated with the development of NEC [28]. Although the link between PDA and NEC is well established where outcome is incidence of NEC, the contribution of PDA to NEC-related mortality is not well characterized.

NEC prevention and treatment continues to challenge neonatologists and pediatric surgeons despite active research efforts. Rising health care costs and growing momentum for state-based universal health care coverage makes it imperative to understand neonatal ailments that may lead to chronic costly conditions. Since California is a large, diversely populated state, we felt it was an ideal setting to determine the patient- and institutional-based disparities associated with a devastating neonatal condition. Disparities in infant mortality are primarily determined by access to specialized health care [29]. Recent evidence from California showed that there are differences in adult patient characteristics such as race/ethnicity and insurance status that affect surgical care received at high-volume hospitals [30]. Little is known about potential institutional- or patient-based disparities that may exist for NEC. Most health care service research focuses on identifying patient-based factors such as race/ethnicity, gender, education, etc. A more complete approach as outlined by Kilbourn *et al.* involves a systematic approach of identifying disparities by stratifying outcomes to patient factors, clinical encounter, and provider factors [31]. To that end, we sought to determine the influence of patient-specific treatment and institutional-based factors on NEC outcomes. We employed the Kilbourn disparity model [31] in analyzing hospital discharge data in California over a 6-y period.

METHODS

Data Source

We used the California Office of Statewide Health Planning and Development (OSHPD) inpatient hospital discharge database in this study. Numerous investigators analyzed this database to investigate various health conditions [30, 32–38]. Administrators at California licensed hospitals submit information regarding every discharge from their respective facilities to the State. The study period was from January 1, 1999 to December 31, 2004. We categorized neonatal intensive care units (NICUs) based on the American Academy of Pediatrics (AAP) California Directory of Neonatal Intensive Care Units, Neonatologists and Perinatologists (October 2006 version) by OSHPD hospital identification numbers assigned to each institution, a method commonly used by other investigators [32–34, 39]. We defined and grouped NICUs as follows: level I (institution with a nursery but without neonatal intensive care); level IIA (no mechanical ventilation); IIB (brief duration of mechanical ventilation); level IIIA (able to care for infants birth weight $>$ 1000 g and gestational age $>$ 28 wk, and only capable of conventional mechanical ventilation); level IIIB (able to provide comprehensive care for extremely low birth weight infants or infants with 28 or less wk gestation); and the highest level designation level IIIC (able to provide ECMO and surgical repair of serious congenital cardiac malformations that require cardiopulmonary bypass) [40]. Median household income per zip code for the state of California was obtained from 1999 U.S. Census using the DataFerrett* application. We then linked median household income data to the OSHPD database according to parental billing zip code [5, 30].

Analytical Strategy and Inclusion Criteria

With regards to NEC-specific outcomes, we chose to analyze the OSHPD data rather than a national dataset [5, 6, 41, 42], as we sought to capture local disparity paradigms. With the hypothesis that NEC outcomes are affected by patient- and/or institution-specific factors, we analyzed the data in an exploratory manner (Fig. 1). We first determined the contribution of patient-specific factors to NEC-related mortality such as gender, race/ethnicity, socioeconomic status, and patient comorbidities (PDA). Second, we stratified the data by health care-specific factors, including NICU levels of care, treatment type (surgical or medical), admission status (inborn or outborn) and admission quarter. We utilized length of stay (LOS) as a secondary endpoint.

We extracted all birth hospitalizations from the database using the OSHPD-specific newborn code and stratified according to the International Classification of Disease, 9th Revision Clinical Modification (ICD-9-CM) for relevant procedure and diagnosis codes. We determined the NEC cohort by using the diagnosis code 777.5. Surgically treated NEC patients were identified with procedure codes 45.0–46.99. From this range of procedure codes, we excluded codes that would not be a part of an operative procedure for NEC. Procedure codes that were included in the range of 45.0–46.99 were restricted to be specific for exploratory laparotomy (45.0, 45.00), bowel resection (45.02–3. 45.1, 45.29, 45.3–4, 45.41, 45.49, 45.50–2, 45.6–63, 45.7–79,45.8, 46.99), stoma creation (46.0–46.64), and intestinal anastomosis (45.9–94, 46.73–79, 46.93–4). PDA was identified with diagnostic code 747.0 and the PDA ligation with procedure code 38.85. We identified birth weight with the following ICD-9-CM codes: 764.0–764.99, 765.01–765-19, and V21.31–21.35.

Explanatory Variables

OSHPD categorizes ethnicity as Hispanic, non-Hispanic or Unknown. Race is coded as White, Black, Native (American/Eskimo/Aleut), Asian, Other, and unknown. As commonly done in the literature [5, 30, 34, 35, 39], we treated race and ethnicity as a single variable and subcategorized them as Hispanic White (Hispanic), Non-Hispanic White (White), Black, and Asian. We included Hispanic Asian, Hispanic Black, Pacific Islander, and Native populations (Native American/Eskimo/Aleut) groups in the Other category since the sample size was less than 1% of the overall NEC cohort. To identify economic and institutional health care disparities, we analyzed NEC mortality according to insurance status (state-based funding such as Medi-Cal *versus* HMO/private coverage), level of NICU care and admission source defined as either inborn (patient care in the birth hospital) or outborn (patients born at another institution and transferred for further care to the hospital of discharge). In addition, we investigated whether parental income could be related to mortality. Based on the distribution of the median household income per billing zip code for the neonates, we dichotomized median household income as less than $30,000 and greater than or equal to $30,000. To have a surrogate for comorbidities that directly correlated risk of death, we included the variable number of ICD-9-CM diagnoses

*Census data was obtained from U.S. Census Bureau using Data Ferrett application (dataferrett.census.gov).