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Immunization Status of NICU Graduates at a Tertiary Care Children's Hospital

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ABSTRACT

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Background: The objectives of this study were to determine the current rates of immunization and identify variables associated with immunizations of NICU graduates who were 60 days of age or older at time of discharge.

Methods: This is a descriptive pilot study utilizing retrospective paper chart review. The relationships between immunization status and study variables were examined using logistic regression.

Results: Of 43 infants discharged at least 60 days of age or older from the NICU, 74.4% were up to date for immunizations in accordance with AAP recommendations. Additional variables were not significant.

Conclusion: Immunization needs to be a priority in order to give NICU infants every advantage regarding their future health status.

Key Words: NICU, preterm, immunizations

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Immunization Status of NICU Graduates at a Tertiary Care Children's Hospital

In the United States, approximately 500,000 infants are born prematurely each year (Centers for Disease Control and Prevention [CDC], 2013). Prematurity is defined as a gestational age prior to 37 weeks (CDC, 2013). The last few weeks of gestation are the most important for establishing immunological health in an unborn child. As the fetus reaches the third trimester, immunoglobulin G (IgG) maternal/fetal transfer increases. IgG-immunoglobins circulate through the blood and include the most common antibodies responsible for initial phagocytic destruction of foreign microorganisms. IgG immunoglubins pass from mother to child through the placenta (Resch, 2014; Zanetti, 2013). Because this transfer occurs predominantly in the third trimester, infants born prior to 37 weeks do not receive the immunological benefits of this transfer to the same extent as infants carried to full-term and, as a result, are born with a poor immunological status (Gad & Shah, 2007). Additionally, delayed access to or deprivation of breast milk, which provides passive immunity both for bacterial and viral organisms, can contribute to poor immunological status and impaired immunological memory in premature infants (Gad & Shah, 2007).

Immunological memory is the ability of the body's immune system to recognize previously encountered antigens and pathogens and form a specific response to that antigen or pathogen. Having been previously exposed to an antigen or pathogen allows a person to have a more expeditious response with less severe reaction (Resch, 2014; Zanetti, 2013). Thus, immunological memory is a necessary building block for a healthy immune system. Infants with an impaired immunological memory can be compromised and subject to immunosuppression (Gad & Shah, 2007). Therefore, infants born even a few weeks early are at increased risk for

developing severe symptoms from vaccine-preventable diseases because they are less likely to have received crucial IgG that is transferred from the mother (CDC, 2013; Teune et al., 2011).

The American Association of Pediatrics (AAP) recommends clinically stable preterm and low birth weight (LBW) infants receive all immunizations at the same chronologic age as full-term infants, regardless of gestational age or weight at birth (Saari, & Committee on Infectious Diseases, 2003). Under the AAP guidelines, at 60 days of age, an infant should receive Diphtheria and Tetanus and Pertussis (DTaP), Haemophilus Influenza Type b (Hib), Polio vaccine (IVP), and Hepatits B (Hep B) (Saari, & Committee on Infectious Diseases, 2003).

However, AAP and CDC recommendations for Hep B are contingent on infant weight and maternal Hepatitis B surface antigen (HBsAg) status. If the mother's HBsAg is positive or unknown the infant should receive Hepatitis B immune globulin (HBIG) and a single- antigen Hep B vaccination within 12 hours of birth regardless of weight. If the infant weighs less than 2000g and if the mother's HBsAg is negative, the first dose of Hep B should not be administered until one month of age or at discharge (CDC, 2015).

Despite AAP recommendations, many health care providers (HCP) delay administration of immunizations to preterm infants (Batra et al., 2009; Navar-Boggan, Halsey, Escovar, Golden, & Klein, 2012). Langkamp and Langhough (1992, 1993) found that many physicians believe factors such as birth weight and degree of prematurity should influence the timing of immunizations, indicating that many HCP lack knowledge concerning AAP immunization recommendations. Batra et al. (2009) found immunization rates were 3% to 15% lower for LBW infants and 17% to 35% lower for very low birth weight (VLBW) infants compared to normal birth weight (NBW) infants. Only 87% of extremely low birth weight (ELBW) infants had up to date immunizations as compared to 92% of LBW and NBW infants. Birth weight is defined as,

"extremely low birth weight [ELBW]: <1000g; very low birth weight [VLBW]: 1000-1499g; low birth weight [LBW]: 1500-2499g and normal birth weight>or equal to 2500g" (Batra et al., 2009, p. 952).

Additionally, many infants in newborn intensive care units (NICU) are not immunized in accordance with AAP guidelines. Navar-Boggan et al. (2012) reported that only 51% of infants discharged from a NICU were up to date for routine immunizations and 27% had received no immunizations. Additionally, Woestenberg et al. (2014) reported that DTaP and IPV vaccinations were given later then recommended in 25% LB, 33% of VLBW, and 44% of ELBW infants. The vaccination rate of premature infants and NICU infants is suboptimal. Delayed or non-immunization additionally is linked to an increased risk for delayed immunizations at later ages (Langkamp, Hoshaw-Woodard, Boye, & Lemeshow, 2001; Navar-Boggan et al., 2012; Tozzi et al., 2014; Woestenberg et al. 2014).

The purpose of this study was to determine immunization rates of infants 60 days of age and over who were discharged from a tertiary children's hospital NICU. A secondary purpose of this study was to identify potential risk factors for non- or under-immunized NICU graduates.

Research Questions

1. What are the current rates of immunization of NICU graduates who are 60 days of age or older at time of discharge?
2. What variables are associated with immunization of NICU graduates who are 60 days of age or older at time of discharge?

Methods

This is a descriptive pilot study utilizing retrospective chart review. Institutional Review Board approval and a waiver of informed consent were obtained prior to data collection. The

research team collected data using paper records from the NICU in a tertiary care children's hospital. The team reviewed charts onsite and did not gather identifiable patient data.

Sample and Setting

The setting was a 52-bed NICU in a tertiary children's hospital that services a large geographic area in the intermountain West. The sample was comprised of paper charts for infants 60 days of age or older who had been discharged from the NICU between January 1, 2012 and December 31, 2013. Staff from the medical records department identified 56 charts that met inclusion criteria. Two research team members reviewed the selected charts to ensure inclusion criteria were met. Ten charts were excluded due to infants being greater than 60 days of age at the time of transfer to the local NICU. One chart was excluded because the infant was discharged prior to 60 days of age. An additional two charts were excluded due to incomplete data. A total of 43 charts were included in this study.

Instrument

The research team entered de-identified data directly into a cloud-based data repository. The team assessed hospital records for children 60 days of age or older who were discharged for the following data in nine specific perceptions of vulnerability: (1) gestational age at birth, (2) age at discharge, (3) whether discharge occurred during flu/RSV season, (4) birth weight, (5) APGAR scores, (6) gender, (7) medical complications (8) a diagnosis of bronco-pulmonary dysplasia (BPD), (9) a diagnosis of retinopathy of prematurity (ROP) and, medications and immunization records.

Data Analysis

Data were analyzed using SPSS version 22. Data were examined for missing values and outliers using descriptive statistics and appropriate figures. Descriptive statistics were calculated

for all variables. Relationships between study variables and immunization status were examined using chi-square tests and logistic regression.

Results

Table 1 shows descriptive statistics for demographic characteristics and study variables. The mean gestational age of babies that met inclusion criteria was 32 weeks 6 days with a standard deviation of 4 weeks 6 days. Slightly less than half were female—19 of the 45 babies (44.2%). Mean birth weight was 2009.2 grams with a standard deviation of 1084.5 grams. APGAR scores at one minute had a mean of 4.6 with a standard deviation of 2.8. APGAR scores at five minutes increased to a mean of 6.6 with a standard deviation of 2.5. A majority of infants—35 out of 43 (81.4%)—had a positive blood culture or infection at some point while admitted to the NICU. Approximately one-third of the infants had diagnoses of apnea and bradycardia (A&B) (15 infants, 34.9%), patent ductus arteriorsis (PDA) (14 infants, 32.6%), ROP (11 infants, 25.6%), or BPD (6 infants, 14.0%). Most infants—33 (73.8%)—had two or fewer of the preceding diagnoses, while the remaining infants—10 (23.3%)—had three or more. Most of the infants—39 (90.7%)—required some form of respiratory assistance (intubation, CPAP, or high-flow nasal cannula).

Most infants—34 of 43 (79.1%)—received at least one immunization before discharge. All but 2 of 34 (4.7%) infants received all four scheduled immunizations (DTaP, Hep B, Hib, & IVP), and those 2 infants did not receive the IVP immunization.

Receiving any form of respiratory assistance was not significantly associated with not being immunized. Having a diagnosis of A&B, PDA, BPD, ROP, or positive blood culture or infection was not significantly associated with not being immunized. There was no association between gender and immunization status.

A logistic regression then assessed predictors of being immunized before discharge from the NICU. Predictors included in the regression were gestational age, birth weight, gender, and age at discharge. The regression did not include diagnoses and interventions since none of them demonstrated a significant relationship with being immunized during a preliminary analysis. A backward Wald method removed non-significant predictors from the model. The beginning block percent correct classification was 79.1%. The omnibus test of model coefficients was significant χ^2 (df=1) = 13.203, $p < .001$ indicating the model is acceptable. The Cox & Snell R^2 = .264 and the Nagelkerke R^2 = .412 indicating age at discharge explains between 26.4% and 41.2% of the variance in immunization. The Hosmer and Lemeshow Test was not significant χ^2 (df=8) = 2.807, p = .946 indicating the model is not significantly different from the data. The only predictor which was significant was age at discharge B=.56, SE=.261, Wald=4.626, df=1, p=.031, Exp(B)=1.751, 95% CI Exp(B) [1.051, 2.919]. The logistic regression found that for every 1 week increase in age at discharge, infants were 1.75 times more likely to be immunized before discharge.

Discussion

Approximately three-fourths of the NICU infants in the study received immunizations according to the AAP recommendations. This percentage was incongruent to the limited findings available specific to NICU infants and immunization rates (Gad & Shah, 2007; Navar-Boggan et al., 2012). Navar-Boggan et al. (2012) reported 49% of subjects were not up to date for 2 months immunizations in the NICU. However, Batra et al. (2009) found that infant immunization rates, in regard to birth weight only, was the same or higher than in this study. Batra et al. (2009) found immunization rates for ELBW through NBW ranged from 70-97.3% at two months of age (Batra et al., 2009).

Significantly, data from this study, showed infants discharged at 55 to 70 days of age were more likely to be immunized. This is logical, considering two month immunizations should take place at 60 days of age. However, perceptions of vulnerability were not found to be significant factors predicting the immunization of NICU infants. In spite of positive age related associations, Gad and Shah (2007) cited reasons such as parental concerns and inadequate discharge planning as reasons for decreased immunization rates of NICU infants. Navar-Boggan et al. (2012) reported NICU infants with medical factors such as congenital heart disease, BPD, and A&B were more likely to be immunized than infants who received surgery during their stay in the NICU.

Parents who did not allow the immunization of their NICU infants were concerned that their infants were at greater risk for autism spectrum disorder, sudden infant death syndrome, and learning disabilities (Gad & Shah, 2007). Studies indicate that immunizations should be administered in the NICU to allow for 48 to 72 hours for post-immunization monitoring (Gad & Shah, 2007; Navar-Boggan, Halsey, Escovar, Golden, & Klein, 2010; Saari, & Committee on Infectious Diseases 2003). Paradoxically, HCPs' may hesitate to administer immunizations fearing post-immunization reactions such as fever, apnea, bradycardia, or sepsis (Navar-Boggan et al., 2010, 2012). Parents' or HCPs' perceptions of vulnerability, such as poor medical conditions, may delay the administration of immunizations to NICU infants (Navar-Boggan et al., 2012). However, not administering immunizations in the NICU, according to AAP recommendations, is shortsighted. Parents and providers need to consider the risks involved when a premature patient has an adverse reaction to a vaccine in a non-hospital setting; adverse reactions may require a premature infant to be readmitted to the hospital for further care.

Limitations

This study, like all studies, has limitations that need to be addressed in future research. Because labor and delivery records were not available, the research team's examination was limited to what was available in an infant's medical record. Occasionally, an infant's record did not include information from the transferring facility**.** The study made no distinction between death, discharge to home, or transfer to another facility. Chronic lung disorder (CLD) was occasionally used interchangeably with BPD, additionally; CLD was also used to describe other lung diseases. Hence, this discrepancy may have led to incorrect data collection regarding lung disease. This is a pilot study that includes two years' of data from a small sample at one institution and may not be generalizable. Data regarding rotavirus and pneumococcal virus vaccines was not gathered.

Recommendations for Future Research

Both quantitative and qualitative research questions need to be addressed in future research. Future studies should focus on larger samples from diverse hospitals and levels of NICUs. Additionally, future studies should incorporate discharge information. Information regarding timing of immunizations in relation to discharge date could enhance understanding about adverse reactions and immunizations. Qualitative studies exploring and describing provider knowledge of current AAP guidelines will strengthen our understanding of potential barriers to immunization. Studies exploring provider and caregiver beliefs regarding immunizations of premature and LBW infants could encourage dialogue and educational opportunities.

Conclusion

Preterm infants are at increased risk for vaccine preventable diseases due to poor immunological status. AAP recommends that 2-month immunizations be given at 60 days of age regardless of gestational age or weight at birth. This study found that three-fourths of the subjects were properly immunized when discharged from a NICU at 60 days of age or older. Infants that leave the NICU unimmunized or under immunized often continue to be underimmunized during the first year of life and remain significantly less likely to have completed the recommended vaccination schedule by 36 months of age (Batra, 2009; Langkamp, et al., 2001). Parental and HCP lack of knowledge of AAP recommendations, may play a role in lower immunization rates of NICU infants. Immunization needs to be a priority in order to give NICU infants every advantage.

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Table 1

Demographic Characteristics

Variable	N (%)	Mean (SD)
Gestational Age (days)		230.1 (34.7) 32 weeks 6 days (4 weeks 6 days)
Age at Discharge (days)		112.9 (60.3)
Gender		
Female	19 (44.2%)	
Male	24 (55.8%)	
Birth Weight (grams)		2009.2 (1084.5)
Discharge/Death between 55 - 70 days of age		
Yes	8 (18.6%)	
No	35 (81.4%)	
Discharge During Flu Season		
Yes	15 (34.9%)	
No	28 (65.1%)	
Apgar (1 minute, n=40)		4.6 (2.8)
Apgar (5 minute, n=41)		6.6 (2.5)
Apgar (10 minute, n=27)		7.9 (2.5)
Apnea & Bradycardia		
Yes	15 (34.9%)	
No	27 (62.8%)	
Patent Ductus Arteriousus		
Yes	14 (32.6%)	
No	29 (67.4%)	
Broncho-Pulmonary Dysplasia		
Yes	6 (14.0%)	
No	37 (86.0%)	
Retinopathy of Prematurity		
Yes	11 (25.6%)	
No	32 (74.4%)	

Demographic Characteristics

Variable	N (%)	Mean (SD)
Positive Blood Culture or Infection		
Yes	35 (81.4%)	
No	8 (18.6%)	
Number of Diagnoses		
0	2 (4.7%)	
1	16 (34.2%)	
2	15 (34.9%)	
3	7 (16.3%)	
4	1 (2.3%)	
5	2 (4.7%)	
Respiratory Assist		
Yes	39 (90.7%)	
No	4 (9.3%)	
Intubated		
Yes	37 (86.0%)	
No	6 (14.0%)	
Intubated Days		30.6 (32.1)
CPAP		
Yes	20 (46.5%)	
No	23 (53.5%)	
CPAP Days		11.2 (10.8)
High Flow Nasal Cannula Days		
Yes	30 (69.8%)	
No	13 (30.2%)	
High Flow NC Days		20.3 (18.8)
Corticosteroids within 14 Days of Discharge		
Yes	9 (20.9%)	
No	34 (79.1%)	

Demographic Characteristics

Variable	N (%)	Mean (SD)
TDaP		
Yes	34 (79.1%)	
No	9 (20.9%)	
Hep B		
Yes	34 (79.1%)	
No	9 (20.9%)	
Hib		
Yes	34 (79.1%)	
No	9 (20.9%)	
IVP		
Yes	32 (74.4%)	
No	11 (25.6%)	
Number of Immunizations		
0	9 (20.9%)	
1		
2		
3	2 (4.7%)	
4	32 (74.4%)	
Immunization Age (days)		61.5 (46.6)