IDENTIFYING PREDICTORS FOR PERTUSSIS DISEASE IN TEXAS INFANTS UTILIZING SURVEILLANCE RECORDS AND BIRTH CERTIFICATE DATA FROM 1999-2003

THESIS

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DEDICATION

This thesis is dedicated to my amazing parents, Petesio and Maria Palenapa. Thank you for your unfailing love and support throughout the years. I am truly blessed to have your love and guidance. I cannot begin to express my gratitude for everything you have done for me. I love you both.

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Using a retrospective case-control design, this study investigated possible risk factors for the development of disease by matching pertussis surveillance data from 1999 to 2003 to birth certificate data. The aim of this study was to identify significant risk factors for the development of pertussis by analyzing infant, maternal, and paternal variables available through birth certificate data. Cases were established through the matching of pertussis disease surveillance to appropriate birth certificate data. A 3:1 control group was created by matching date of birth and pulling birth certificate data for comparison. Multivariate logistic regression statistical techniques were applied in analysis of data. When analysis was completed, 6 out of 16 variables selected for data analysis were found to be significant with adjusted odds ratios greater than the value of 2. The six significant predictors were number of siblings living ≥ 5 (OR=3.1, 95% CI 1.4-7.2), paternal age ≤ 19 (OR=2.9, 95% CI 1.7-5.1), paternal educational level of >12 and ≤ 15 years (OR=2.4, 95% CI 1.5-3.8), infant birth type of multiple (OR=2.2, 95% CI 1.1-4.4), infant birth weight 1500-2499 grams (OR=2.2, 95% CI 1.3-3.7), and mother's cigarette use (OR=2.3, 95% CI 1.3-3.5). Overall, this study showed evidence that the odds of pertussis infection in infants increased as number of siblings increased. Infants with five or more siblings were over three times as likely to develop pertussis than infants without siblings. Younger paternal age and mother's cigarette use also demonstrated increased odds for infants to develop pertussis infection. The elevated risk effect for all six significant predictors is large enough that further study is warranted to investigate the effect of these variables on pertussis development in infants.

CHAPTER 1

INTRODUCTION

Pertussis, better known as whooping cough, is a highly infectious respiratory disease caused by the bacterium *Bordetella pertussis (B. pertussis)*. Despite the availability of vaccines to prevent its occurrence and spread, the number of pertussis cases being reported in the United States as well as in Texas continues to rise. In fact, reports of pertussis disease throughout both the nation and state of Texas are currently at a 40-year high (National Center for Health Statistics (NCHS), 2004). This resurgence in pertussis demonstrates the need for new measures to control and reduce the further spread of the disease. In order to accomplish this feat, new measures are needed to reduce the spread of pertussis. One approach to reducing the spread of disease would be to establish statistically significant predictors of pertussis infection among those who have had the disease and utilize these indicators in aiding clinicians in earlier identification of the illness. By identifying the illness earlier, clinicians may be able to provide earlier treatment to reduce the severity of disease and earlier prophylaxis to contacts in order to reduce further spread.

Although this illness affects people of all ages, the disease burden is most serious in infants. Many infants who are infected with pertussis are too young to receive the vaccine and are not protected against the disease. Infants with pertussis suffer a long list of severe complications including sinusitis, pneumonia, physical sequelae of paroxysmal cough, subcutaneous emphysema, pneumothorax, umbilical inguinal hernias, rectal prolapse, encephalopathy and even death (Cherry & Heininger, 1998). For these reasons, new preventive measures are needed to reduce the spread of pertussis in its most vulnerable cohort; infants less than one year of age.

Determining possible predictors for pertussis in infants would provide crucial information to clinicians in order to aid in earlier diagnosis and prophylaxis to fight the disease and any sequelae. Useful predictors might include characteristics of infants who were infected with pertussis as well as characteristics of their parents. Surveillance data on such infants are available through the Texas Department of State Health Services (DSHS), as pertussis is mandated as a notifiable disease condition.

Past studies have also utilized birth certificate data to ascertain characteristics of various communicable diseases including predictors of disease. The Texas Department of State Health Services (DSHS) has used vital statistics data to assess the immunization status of children born to human immunodeficiency virus-infected mothers, assess the under immunization of Texas children reported as measles cases and assess risk factors for congenital syphilis (Pelosi & Schulte, 2003). Birth certificate data have been successfully used to assist in the education, prevention and continued surveillance of infectious diseases. Birth certificate data from DSHS provides a comprehensive source from which to obtain timely infant, maternal and paternal data characteristics that are descriptive of a family within one year's time of the infant's birth. Linking birth certificate data with pertussis surveillance data may provide insightful details to predictors of disease among infants less than 12 months of age in Texas. Identifying predictors of pertussis disease can assist in the prevention and early diagnosis of pertussis and consequently enhance surveillance and reporting methods.

Background

Pertussis vaccines were introduced in the United States in the 1940s as part of a combination vaccine, which also protected against diphtheria and tetanus. Within 30 years of the introduction of pertussis vaccines, a reduction of 99% of the disease was achieved and reported cases declined to an all time low throughout the nation (Billeter, 2006). Although pertussis vaccine coverage continues to maintain high immunization levels in the country today, pertussis incidence has experienced a steady resurgence in the last two decades (Crowcroft & Pebody, 2006; Raguckas, VandenBussche, Jacobs & Klepser, 2007; Tanaka et al., 2003). In 2005, Texas experienced a marked pertussis surge with 2,224 reported cases and an incidence rate of 9.6 per 100,000. Texas has not witnessed incidence rates as high as this since 1967 (DSHS, 2006). With such an alarming increase in the disease, the necessity for new strategies and preventative measures in order to combat and reduce the spread of pertussis is reemphasized.

Because pertussis is a vaccine-preventable disease with an established method for prevention, a vaccine with average efficacy rates of 84%, little research has been done on pertussis disease predictors in the past (Bisgard et al., 2004). A great deal of previous pertussis literature exists in other areas of interest. A large percentage of earlier research conducted on pertussis was mainly concentrated in vaccine safety, efficacy and immunogenicity issues. Other research dealt with the epidemiology of pertussis including history and trends. Disease burden and economic burden have also been described and evaluated. Most recent literature on pertussis deals with recommendations for a new booster vaccine now available to adolescents and adults and strategies for reducing disease incidence. However, no published research has attempted to find pertussis disease predictors through the use of birth certificate data and surveillance data as in this study.

Two previous studies have been conducted to investigate predictors for pertussis disease in infants. First, a case-control study was created to review findings from a pertussis outbreak in Chicago in 1993. Although cases and controls had similar pertussis vaccination coverage levels of 87% and 89% respectively, two significant risk factors for pertussis development in infants were identified; young maternal age and mothers who had a cough lasting seven days or more (Izurieta et al., 1996).

The second research study involving analysis of pertussis predictors for infant deaths was conducted in 2005 by the National Institute for Public Health Surveillance in France. Data were collected from a national pertussis surveillance network and risk factors were investigated for a decreased risk of severe childhood pertussis (Briand, Bonmarin & Levy-Bruhl, 2007). Results found that infants who had received the first dose of vaccine and were seen late in the course of illness had decreased risks of developing severe disease. Inversely, this study found that infants who had not yet received vaccine and infants seen earlier in the course of illness were at an increased risk of developing severe disease. Theoretically, infants seen earlier should lead to an earlier diagnosis; it is important to understand that young infants are often non-symptomatic. Additionally, the beginning stages of pertussis often mimic symptoms common in the early stages of a cold. In summary, the combined predictors identified in both studies were young maternal age, mothers who experienced a cough of seven days or more, infants who had not received vaccine and infants who were seen earlier in the course of the illness.

Four more similar studies evaluated pertussis predictors for death in infants. First, a case-control study of deaths was matched with nonfatal cases. Using stepwise logistic regression, analysis results uncovered two independent predictors for fatal pertussis; white blood cell count and pneumonia (Mikelova, Halperin, Scheifele, Smith, Ford-Jones & Vaudry, 2003). Patients with leukocytosis, abnormally elevated white blood cell counts, and those who had suffered pneumonia were at increased likelihoods for rapid and fatal progression of pertussis.

A second study conducted by the Centers for Disease Control and Prevention (CDC) compared pertussis deaths from the 1990s with deaths from the 1980s (Vitek, Pascual, Baughman & Murphy, 2003). This study established several important findings; risk factors for death included Hispanic race and a gestational age of less than 37 weeks. Vitek et al. (2003) found that a disproportionate share of deaths were complicated by pulmonary hypertension.

A third research study conducted a retrospective review of all pertussis deaths from 1992 and 1993 by collecting discharge summaries and autopsy reports. This study found two variables to be consistent with almost all infant pertussis deaths; young maternal age and pre-term delivery (Wortis, Strebel & Wharton et al., 1996). Wortis et al. (1996) found results that further supported the findings of Izurieta et al. (1996) which concluded that young maternal age was a significant predictor for pertussis.

In the fourth study, Pelosi and Schulte (2003) examined Texas birth certificate data in an attempt to identify significant maternal and pediatric characteristics that would predict under-immunization or hospitalization for pertussis. Pelosi and Schulte were unable to identify any significant predictors. In summary, significant predictors of pertussis death in an infant from these studies were white blood cell count, pneumonia, Hispanic race, gestational age less than 37 weeks, young maternal age and pre-term delivery.

In concatenating risk factors for both pertussis disease and pertussis death, the following predictors were identified: young maternal age, mothers who experienced a cough of seven days or more, infants who had not received vaccine, infants who were seen earlier in the course of the illness, white blood cell count, pneumonia, Hispanic race, gestational age, and pre-term delivery. Of these predictors, young maternal age, Hispanic race, gestational age and pre-term delivery may be observed through Texas birth certificate data. It is important to note that none of these predictors were yielded through study of Texas data. Analysis of Texas data may or may not reveal similar results.

With pertussis cases on the rise, the complexity of the disease presents an important challenge to public health professionals and the medical community. One major issue includes laboratory testing procedures to detect pertussis. Current diagnostic tests approved by the Food & Drug Administration (FDA) have low sensitivity, do not function optimally, and are not reliable methods for ruling out disease (Lievano et al., 2002; Mattoo & Cherry, 2005). A second issue includes non-recognition and misdiagnosis of pertussis by clinicians. Pertussis is automatically ruled out by many clinicians based on a patient having had the pertussis vaccine (Deeks, DeSerres, Boulianne, Duval, Rochette, Dery, et al., 1999). Prior vaccination should not rule out pertussis diagnosis because the vaccine is not 100% effective (National Network for

Immunization Information (NNii), 2008). Also, because symptoms of pertussis are similar to a cold, it is often misdiagnosed. A third major constraint concerns waning immunity levels to pertussis. Adolescents and adults who were previously completely immunized may experience waning of their immunity to pertussis. Research has found that pertussis immunity lasts for an average of 10 years (Wendelboe, VanRie, Salmaso & Englund, 2005). A new pertussis booster for adolescents and adults was recently introduced to help combat this issue. These elements of difficulty combined contribute to pertussis being the least well-controlled vaccine-preventable illness for most developed countries in the world (Cherry, Grimpel, Guiso, Heininger & Mertsola, 2005).

Primary prevention methods for pertussis include vaccinating infants and children. Current recommendations for vaccinations in infants and children include five doses of DTaP (diphtheria tetanus and acellular pertussis) at 2, 4, 6, and 12 months of age with one more dose to be given between ages four through six years. DtaP vaccine is 95% effective in protecting against all three diseases that it immunizes against (Ward, et al., 2005).

A new booster vaccine for adolescents and adults was approved by the U.S. Food & Drug Administration (FDA) and introduced to the U.S. in 2006. This booster vaccine was implemented in order to boost waning immunity in adolescents and adults. Tdap (tetanus, diphtheria, and acellular pertussis) vaccine can be used to substitute one regular Td (tetanus diphtheria) vaccine dose, which is recommended every ten years. Because infants often are exposed to pertussis through older household contacts including siblings and parents (Crowcroft & Pebody, 2006), Tdap administration to these individuals is essential to fighting the spread of pertussis. New vaccines for adolescents and adults are proven to be safe, effective, and cost-beneficial. In fact, Tdap vaccine is 86 % to 95 % effective in preventing disease in adolescents and 83% to 94 % effective in adults (Ward, et al., 2005). Past research has shown that pertussis has high secondary attack rates in households, as high as 80% in susceptible individuals (Heininger, 2001). These findings demonstrate the importance of preventing pertussis, especially in households with infants and young children. Vaccination of adolescents and adults is instrumental in reducing the overall spread of the disease, especially transmission to susceptible infants (Yeh & Mink, 2006).

Studies on the cost-burden impact of pertussis disease have found significant costs to households. A study in 2000 found the average total medical cost for one pertussis case in a family to average about US $2,822 (Lee & Pichichero, 2000) per case for infants who were younger than 24 months and US $181 for adults. Another study conducted in Germany estimated a non-hospitalized pertussis case to average US $135 (Tormans, Van Doorslaer, van Damme & Schmitt, 1998). Tormans et al. (1998) also found that hospitalized cases increased direct costs to US $6337. One additional study estimated the total economic burden in the United States, both direct and indirect in costs to be about US$17 billion over a 10-year period (Purdy, Hay, Botteman & Ward, 2004).

Pertussis causes more than just an economic burden. This disease takes a toll on parents who are caring for an infant infected with pertussis. Past research has revealed that parents suffer from fears that their child may die; they fear for the health of their child and suffer from a tremendous loss of sleep (Jenkins, 1995; Johston, Hill & Anderson, 1985). Parents may also suffer from stress of impending work at their jobs and potential loss of regular income because of sick days taken off to care for their child.

Once thought of as a childhood disease near eradication, pertussis has reestablished itself as a deadly disease requiring intervention. Clearly, prevention and diagnosis tools and methods for the detection of pertussis still need further development. While vaccination is the best prevention method for pertussis disease, predictors still need to be identified to assist those infants too young to be vaccinated or those not fully vaccinated.

Objective

The purpose of this study was to identify significant risk factors for the development of pertussis disease in infants less than 12 months of age in Texas. This was accomplished by utilizing DSHS pertussis surveillance records and Texas birth certificate data for infants born from 1999-2003. The null hypothesis for this analysis is that no birth certificate data variable will be a significant predictor for pertussis disease.

Benefits of the Study

The finding of significant predictors for pertussis in Texas can provide many benefits to Texas. One of the main benefits of this study is to provide valuable education to the medical community and provide for earlier diagnosis of infants along with appropriate prophylaxis treatments for contacts. Any significant risk factors identified through this study may aid in the development of interventions, which reduce the number of complications and fatalities due to infant pertussis in Texas.

This study aids clinicians, and also provides key data to public health workers who perform pertussis case management duties. Study findings may contribute to the revision of case definitions and classifications for disease or lead to the development of necessary policy updates. Vaccine requirements in schools and day cares may need to be strengthened as a result of findings. With new pertussis prevention policies in place, the number of pertussis-infected individuals may be reduced; in turn decreasing the chance for spread to infants.

Other benefits include providing better steering for the identification of target audiences including age, race, ethnicity, and location. Better-defined target audiences provide for more focused educational prevention campaign efforts. Information gained through this study helps to direct the appropriate allocation of funding for educational campaigns. Data gained through this study also may identify new trends in pertussis disease among different groups.

One last benefit to Texas is a reduction in medical care spending on pertussis. While there are limited studies available on the exact amount of costs related to pertussis, experts agree that the cost for one pertussis case in direct and indirect terms is significant. A decline in pertussis leads to a reduction in dollars spent on medical care and treatment, a reduction in cost to taxpayers for cases that were enrolled in Medicaid, and a reduction in the number of productivity days lost through sick leave.

CHAPTER 2

METHODS

In the state of Texas, surveillance methods for detecting pertussis disease are largely based on passive reporting. By way of the Texas Administrative Code, pertussis is listed as a notifiable disease condition. This means that, by law, clinicians and anyone with knowledge of a suspected pertussis disease case are required to report this within one working day to either their local health authority or state health authority offices. Reports of pertussis are often received from physician offices and also from school nurses, day care centers and parents. Most often these reports are received via telephone report. A large portion of pertussis cases are also reported through positive laboratory results for pertussis. Positive laboratory results are required to be submitted to the state health department, these results are often submitted by electronic copy of HL7-formatted codes, but may also include the faxing of paper laboratory test result copies. All laboratories, including the state laboratory and private laboratories are required to report positive pertussis results. Each suspected case of pertussis is thoroughly investigated by health authorities. Each suspect pertussis investigation is then entered into an electronic disease notification database called the National Electronic Disease Surveillance System (NEDSS). Data elements captured include basic demographic information as well as more detailed information such as whether antibiotics were administered and whether a case was part of an outbreak. An accumulation of pertussis data from across the entire state is submitted electronically on a periodic basis to the Centers for Disease Control and Prevention (CDC) for review.

Pertussis surveillance data for case-infants (pertussis diseased infants) were gathered from the DSHS Infectious Disease Control Unit (IDCU). Birth certificate data for case-infants and control-infants (infants without disease) were collected from the DSHS Vital Statistics Unit (VSU). Case-infants and control-infants consisted of infants born in the state of Texas from 1999 through 2003.

The DSHS Internal Review Board (IRB) granted permission to graduate student, Lucille Palenapa, to access Texas birth certificate data from 1999 through 2003 (see Appendix A). The DSHS IDCU also granted permission to Lucille Palenapa to access data for this research project (see Appendix B). All data were coded and de-identified after linking VSU data to surveillance data. No personal identifiers were included in the data analysis shared for this study. All study data were guarded as highly confidential and treated accordingly.

Research Design

This study was a retrospective case-control study that attempted to identify predictors for the development of pertussis disease in infants less than 12 months of age. Disease surveillance data were utilized to identify diseased cases and establish dates of birth from which control cases would be matched. All predictor variables analyzed for this study were ascertained from birth certificate data.

Study Population

The study population was comprised of infants born in Texas from 1999 through 2003. Case-infants were defined as infants less than 12 months of age who were born in Texas from 1999 through 2003 and were reported to the DSHS as a confirmed or probable case of pertussis, in accordance with CDC case definitions. Over the five-year study time frame, a total of 1,680 diseased infants less than 12 months of age were identified from surveillance records.

Exactly 451 of the 1,680 case-infants were matched from surveillance records to birth certificate data, based on exact birth date, full name and address. Only 26% of eligible case-infants were matched to appropriate birth certificate data and were included in this study. Reasons for case-infants not finding matches in the DSHS birth certificate registry included the possibility of families having changed addresses since infant's birth, misspelling of names, inaccurate record of surveillance record birth dates or the possibility of the case-infant being born outside the state of Texas. Only exact matches were used to ensure integrity of case-infant data.

Control-infants were defined as infants in Texas who had not been reported to the DSHS as having had pertussis. Control-infants were matched by same birth date as case-infants; three control-infants were randomly selected for each case infant. A total of 5,040 infants were found to be eligible to for control selection.

Of the 5,040 possible controls, 1,353 were selected after conducting a randomized selection process using SAS Version 9.0 (SAS Institute, 2007). After concatenating the 451 case-infants and the 1,353 case-controls into one data set, a total of 1,804 records were eligible for analysis. Quality assurance checks were performed before and after matching processes were completed to screen out those ineligible for study.

Exclusion criteria for this study included infants who were not born in Texas or who were older than 12 months of age at the time of illness onset and cases of ruled out pertussis or lost to follow-up cases of pertussis. A twin sibling of a potential control was considered ineligible for use as another control subject. Infants with more than one case of pertussis in the five-year study time frame were only counted once.

Data Collection

Two main sources of data used for this study included birth certificate data and pertussis disease surveillance data. Birth certificate data for 1999-2003 were taken from the DSHS birth registry system. Data extracted from birth certificate included infant, maternal and paternal demographic and characteristic information. Surveillance records were extracted from two systems used by DSHS to submit cases to CDC, the National Electronic Telecommunications System for Surveillance (NETSS) and the NEDSS. Surveillance records were utilized to identify case-infant information. Case-infant information established dates of birth from which birth certificate data could then be matched to randomly select control-infants. Infants less than 12 months of age, identified as confirmed or probable cases of pertussis in accordance with CDC epidemiology guidelines (see Appendix C), were extracted for years 1999-2004. Surveillance data for 2004 were extracted in order to match with 2003 birth cohort data.

Confounding Factors

Randomization and adjustment techniques aided in reducing confounding factors. Reducing confounding factors was necessary in order to avoid a false positive conclusion. A randomized selection process was used to match controls to cases. After multivariate logistic regressions were run and significant predictor variables were identified, variables were then analyzed for confounding by removing variables and observing changes in the odds ratio values. Predictor variables that did not create at least a 10% change in adjusted odds ratio values were removed and those that did create at least a 10% change in odds ratio values were kept in the adjusted model.

Analysis

Eighteen variables were chosen for analysis from the birth certificate data. These variables were chosen based on indications of biological feasibility and on previous epidemiological research studies. Table 1 reflects the 18 variables chosen for analysis, depicted their percentage of data completeness and whether that variable was chosen for further analysis.

Two variables, birth length and whether mother of infant was enrolled in Medicaid, were eliminated because data completeness was less than 50%. Birth length is associated with the development of an infant and Medicaid status could feasibly have a tie to the development of pertussis because Medicaid enrollees are often at a socioeconomic disadvantage and may not have access to or the ability to afford medical care for all household members. Because these variables were eliminated, there was not an opportunity to investigate their association to developing pertussis disease in this data set. Removal of missing variables was necessary because leaving too many arbitrary variables in a regression model can lead to statistical imprecision (Hair, Anderson, Tatham & Black, 1998).

Table 1

Variables Selected for Analysis from Texas Birth Certificates

Variable	% Missing	Selected for analysis (Yes/No)
Infant Characteristic		
Birth length	48.9	No
Birth type	0.0	Yes
Birth sequence	1.9	Yes
Gestational age	1.9	Yes
Number of siblings living	1.0	Yes
Birth Weight	0.1	Yes
Sex	0.0	Yes
Maternal Characteristic		
Age	0.0	Yes
Alcohol Use	0.7	Yes
Education	2.2	Yes
Hispanic origin	0.4	Yes
Marital status	0.1	Yes
Medicaid	67.7	No
Prenatal Care	4.9	Yes
Tobacco Use	0.8	Yes

Table 1 (*continued*)

Variable	% Missing	Selected for analysis (Yes/No)
Paternal Characteristic		
Age	14.7	Yes
Education	16.7	Yes
Hispanic origin	15.0	Yes

Descriptive statistics were conducted to examine whether any differences existed between the maternal and paternal sociodemographic characteristics among cases and controls. SPSS version 12.0 (SPSS Inc., 2002) was used to generate some descriptive statistics. All demographic information for cases and controls were compared for analysis and the differences between proportions was tested by odds ratios using 95% confidence intervals. Potential predictors were analyzed by comparing cases with controls. For each potential predictor, a matched odds ratio and 95% confidence intervals was calculated.

The data set used for analysis contained both categorical and continuous variables. To facilitate further data examination, several continuous variables were analyzed as both continuous and categorical variables. Continuous variables included infant birth weight, infant gestational age, number of siblings living, maternal age and paternal age. Average mean values were calculated with continuous variables. Data were then recoded for analysis in categorical format.

Data consisted of three main groups that included infant, maternal and paternal characteristics. Infant characteristics selected for analysis were birth type, birth sequence, gestational age, number of siblings living, birth weight and sex. The two dichotomous variables, infant birth type and infant sex were categorized appropriately. The variable birth type distinguished between a single versus a multiple birth (twins or more). Examining birth type made biological sense in that twins are sometimes delivered more prematurely than single births. This premature delivery might have affected the infant's immune development. Twin births often have discordant birth weights, with one twin being larger and overall healthier than the smaller twin sibling. Research on twin births found that discordant birth weights lead to mortality rates 11 times higher than non-discordant birth weights (Branum & Schoendorf, 2003). Infant sex was also reviewed to determine if significant gender differences were present among study infants.

The remaining variables were recoded to illustrate important breaks in the data. Infant gestational age was recoded into two respective categories for premature and regular term infants; less than or equal to 37 weeks or greater than or equal to 38 weeks (National Institutes of Health (NIH), 2007). Infant birth weight was recoded into three separate categories; very low birth weight, considered less than 1500 grams; low birth weight, between 1500 and 2500 grams; and above low birth weight, greater than or equal to 2500 grams (CDC, 2007).

Number of siblings living was taken from birth certificate data question, which asked mother to report how many past live births were currently living. The number of siblings living was an important factor to examine because research has shown that larger family size increases the rate of infectious disease spread within a household (Lambert, 1965; Mertsola, 1983). Several studies have also found a strong association with the delay of immunization for pertussis as sibling number increased (Dombkowski, Lantz & Freed, 2004; Reading, Surridge & Adamson, 2004; Schaffer & Szilagyi, 1995).

The variable birth sequence was recoded into two categories, which differentiated between being born first in sequence or not first in sequence. The variable birth sequence in this data denoted the order in which an infant was born. All single births were coded the same as first-born of multiple births. Siblings of multiple births born subsequently were coded according to their arrival. This data set contained 1,746 single births, 57 infants who were part of a twin sibling set and 1 infant born as part of triplet birth.

Maternal characteristic variables included age, alcohol use, education level, Hispanic origin, marital status, prenatal care and cigarette smoking. Dichotomous variables including alcohol use, Hispanic origin, marital status and cigarette smoking were appropriately coded. Continuous variables including age, educational level and prenatal care were recoded. Maternal age was coded into four groups separate groups; mother less than or equal to 19 years of age; those 20 to 29 years of age, mothers 30 to 39 years, and those 40 years of age or older. A young maternal age has been identified in previous literature as being a predictor of pertussis disease (Izurieta et al., 1996). Maternal educational level was recoded to distinguish four distinct levels; mothers who completed middle school or less ($\leq$8 years), high school diploma or less (>8 and $\leq$12 years), high school diploma with some college (>12 and $\leq$15 years), and college graduates ($\geq$16 years). Prenatal care was recoded to distinguish those who received any prenatal care (at least 1 visit or more) versus those who did not receive prenatal care (no visits at all).

Variables for paternal characteristics included age, educational level and Hispanic origin. Hispanic origin, the only dichotomous paternal variable, was appropriately recoded. Paternal age was recoded to distinguish four categories; those fathers less than or equal to 19 years of age, those 20 to 29 years of age, fathers 30 to 39 years, and those 40 years of age or older. Paternal educational level was recoded to distinguish four distinct levels; fathers who completed middle school or less ($\leq$8 years), those with a high school diploma or less (>8 and $\leq$12 years), high school diploma with some college (>12 and $\leq$15 years), and college graduates ($\geq$16 years). Few paternal variables were available through Texas birth certificate for analysis. For this reason, only three paternal characteristics were examined in this study.

A multivariate logistic regression model was used to assess the independent effects of predictors that were found to be important in univariate analyses. Significant predictor variables were identified through odds ratio values greater than a value of 1 and through 95% confidence limits that did not encompass the value of 1. To identify potential confounding, significant predictor variables were finally subject to an odds ratio analysis. The analysis examined the effect of each variable and removed any variables that did not cause at least a 10% change in the odds ratio value of other variables.

CHAPTER 3

RESULTS

Mean value differences for infant, maternal and paternal characteristics among case-infants and control-infants were assessed in Table 2. After converting grams to pounds, case and control infant birth weights yielded mean weight equivalencies of 7.04lbs and 7.32lbs respectively. No noticeable difference in birth weights was evident among case-infants and control infants. Also, no noticeable disparities were observed for the variables gestational age and number of siblings among case-infants and control-infants either.

Case-mother mean values for age and education were slightly lower than control-infant mothers. Mothers of case-infants ranged in age from 14 to 43 years with a mean age of 24.8 years. Control-infant mothers had a mean age of 26.4 years and ranged in age of 13 to 46 years.

Similar to maternal characteristics, case-father mean values for age and education were slightly lower than control-infant fathers. Case-infant fathers ranged in age from 13 to 52 years with a mean age of 27.8 years. Fathers of control-infants had a mean age of 29.6 years and ranged in age from 14 to 66 years.

Table 2

Mean Values of Continuous Variables Describing Infant, Maternal and Paternal Characteristics by Case Status

Variables	Case n=451	Control n=1353
Infant Characteristics		
Birth weight (grams)	3182.6	3306.7
Gestational age (weeks)	38.2	38.5
Number siblings living	1.5	1.7
Maternal Characteristics		
Age (years)	24.8	26.4
Education (years)	11.5	12.3
Paternal Characteristics		
Age (years)	27.8	29.6
Education (years)	11.8	12.4

Maternal and paternal categorical characteristics for cases and controls were described in Table 3. This table covered basic descriptive information that described the characteristics of all study infants' parents. Raw numbers and percentages illustrate the distribution of the categorical variables.

Table 3

Distribution of Categorical Variables Describing Maternal and Paternal Characteristics by Case Status

Variables	Case n=451	Control n=1353
Maternal Characteristics		
Does mother use alcohol?		
Yes	5 (1.1)	8 (0.6)
No	445 (98.9)	1334 (99.4)
Education		
≥12 years	188 (42.7)	414 (31.3)
<12 years	252 (57.2)	911 (68.8)
Is mother of Hispanic origin?		
Yes	242 (54.0)	640 (47.4)
No	206 (45.9)	709 (52.6)
Maternal Status (Mother married?)		
Yes	277 (61.4)	932 (69.0)
No	174 (38.6)	418 (30.9)
Number of prenatal visits		
≥1	420 (97.9)	1264 (98.2)
0	9 (2.1)	23 (1.8)

Table 3 (*continued*)

Variables	Case n=451	Control n=1353
Mother's Race		
White	399 (88.5)	1160 (85.8)
Black	41 (9.1)	146 (10.8)
Native-American	1 (0.2)	1 (0.1)
Asian	9 (2.0)	39 (2.9)
Pacific Islander	0 (0.0)	4 (0.3)
Unknown	1 (0.2)	3 (0.2)
Does mother smoke cigarettes?		
Yes	42 (9.3)	70 (5.2)
No	408 (90.7)	1271 (94.8)
Paternal Characteristics		
Paternal education		
≥12 years	220 (63.0)	834 (72.3)
<12 years	129 (36.9)	319 (27.7)
Is father of Hispanic origin?		
Yes	204 (56.2)	516 (44.1)
No	159 (43.8)	653 (55.9)

Table 3 (*continued*)

Variables	Case n=451	Control n=1353
Paternal Race		
White	327 (72.5)	1013 (74.9)
Black	26 (5.8)	115 (8.5)
Native-American	2 (0.4)	7 (0.5)
Asian	7 (1.6)	36 (2.7)
Pacific Islander	1 (0.2)	1 (0.1)
Unknown	88 (19.5)	181 (13.4)

Roughly 85% of case- and control-mothers in the study were categorized as White. The remaining 15% was respectively made up of Blacks, Asians and others. It is important to note that all mothers who indicated yes to the question of Hispanic origin were categorized in the White race group, except for three individuals. These remaining three mothers were described as being of Black race. Case-infant mothers had a greater percentage of Hispanics than mothers of control-infants. Among mothers with education levels of at least a high school diploma or higher, case-infant mothers actually represented a higher percentage than controls. There were no obvious contrasts in alcohol consumption levels or number of prenatal visits between mothers of cases and controls. A greater number of control-infant mothers were married than were case-infant mothers. One major difference among case and control mothers was observed with the variable cigarette smoking. Among mothers who admitted to smoking cigarettes, case-infant mothers represented nearly twice as many control-infant mothers.

Slightly greater than 70% of case- and control fathers were White, followed by unknowns, Blacks, Asians and others respectively. It is important to note that nearly 20% of case-infant fathers were listed as an unknown race. Additionally, race was unknown for 14% of control-fathers. A greater percentage of case-infant fathers were Hispanic than control-infant fathers. Among fathers who had achieved an education level of high school diploma or greater, control fathers represented a larger percentage. Case-fathers also made up a higher percentage among those who did not graduate high school. These numbers indicated that case-infant fathers were less educated than control-infant fathers.

In order to examine maternal characteristics for infant pertussis more closely, crude odds ratios and 95% confidence intervals were calculated in Table 4. In examining maternal age groups, crude odds ratios for pertussis increased as age decreased when measured against the reference age group of mothers 30-39 years. Mothers who were 19 years of age or less had over twice the odds of having their infant develop pertussis than mothers who were 30 to 39 years of age or older.

In terms of maternal education, mothers with a middle school education or less ($\leq$8 years) and mothers with a high school diploma or less (> 8 and $\leq$12 years) both produced similar and significant odds ratios of 2.1 and 2.2. The reference group in this category was those who completed at least the equivalent of a four-year college degree or higher ($\geq$16 years). These results indicate that as maternal education level decreased, the odds of an infant developing pertussis increased; with the exception of one level consisting of those who completed high school with some college (>12 and ≤15) which yielded lower crude odds of 1.5. Another notable finding was that infants born to mothers who smoked had almost twice the odds, with a crude odds ratio value of 1.9, of developing pertussis in comparison to infants born to mothers who did not smoke.

Table 4

Crude Odds Ratios and 95% Confidence Intervals for Infant Pertussis According to Maternal Characteristics

Variables	Cases n=451	Controls n=1353	Effect OR (95% CI)
Maternal age (years)			
≤19	103	178	2.3 (1.6-3.1)
20-29	238	749	1.2 (0.9-1.6)
30-39	103	401	Referent
≥40	7	25	1.1 (0.5-2.6)
Mother's alcohol use			
Yes	5	8	0.5 (0.2-1.6)
No	445	1334	Referent
Maternal education (years)			
≤8	48	125	2.1 (1.3-3.3)
>8 and ≤12	280	698	2.2 (1.6-3.0)
>12 and ≤15	60	219	1.5 (0.9-2.2)
≥16	52	283	Referent

Table 4 (*continued*)

Variables	Cases n=451	Controls n=1353	Effect OR (95% CI)
Is mother of Hispanic origin?			
Yes	242	640	1.3 (1.1-1.6)
No	206	709	Referent
Mother married			
Yes	277	932	Referent
No	174	418	1.4 (1.1-1.7)
Does mother smoke cigarettes?			
Yes	42	70	1.9 (1.3-2.8)
No	408	1341	Referent

Paternal characteristics for infant pertussis were examined more closely in Table 5 where crude odds ratios and 95% confidence intervals were calculated. Crude odds ratios for paternal age groups followed a trend similar to maternal age groups. With ages 30 to 39 set as the referent age, the results illustrated that as paternal age decreased, the odds of pertussis development increased for infants. Results revealed that a paternal age of less than or equal to 19 years yielded a crude odds ratio value of 2.5 with 95% confidence limits of 1.6 to 3.9 in comparison to fathers of older age groups. Infants with father's less than or equal to 19 years of age were two and a half times more likely to develop pertussis than those infants in the referent group. Additionally, Hispanic fathers had higher odds over non-Hispanic fathers.

In terms of paternal education, fathers with a middle school education or less (≤8 years), fathers with a high school diploma or less (> 8 and ≤12 years) and those who completed a high school diploma with some college (≥12 and <14 years) all produced significant crude odds ratios of 2.1, 2.6 and 2.9. The reference group in this category was those who completed the equivalency of a four-year college degree or higher (≥16 years). As education level increased, the odds for pertussis increased slightly.

Table 5

Crude Odds ratios and 95% Confidence Intervals for Infant Pertussis According to Paternal Characteristics

Variables	Cases n=451	Controls n=1353	Effect OR (95% CI)
Paternal age (years)			
≤19	39	59	2.5 (1.6-3.9)
20-29	182	557	1.2 (0.9-1.6)
30-39	123	462	Referent
≥40	19	97	0.7 (0.4-1.3)
Paternal education (years)			
≤8	33	111	2.1 (1.3-3.6)
>8 and ≤12	213	593	2.6 (1.8-3.7)
>12 and ≤15	62	153	2.9 (1.9-4.5)
≥16	41	296	Referent

Table 5 (*continued*)

Variables	Cases n=451	Controls n=1353	Effect OR (95% CI)
Is father of Hispanic origin?			
Yes	204	516	1.6 (1.3-2.1)
No	159	653	Referent

Crude odds ratios and 95% confidence intervals for infant characteristics are displayed in Table 6. The infant birth weight group of 1500-2499 grams had a higher crude odds ratio over those 1499 grams or less. The reference group in birth weight category was those weighing 2500 grams or more.

Number of siblings yielded a crude odds ratio of 1.3 for those groups comprising 1 to 4 siblings and a crude odds ratio of 2.2 in the group of five or more siblings. This number was in reference to those with no other siblings. As the number of siblings increased, odds of pertussis development increased.

Odds ratio for infant birth type illustrated a difference between single versus multiple births. A birth type of multiple births produced a crude odds ratio of 2.4 over single births. Multiple births had more than twice the chance of single births for developing pertussis. Infants with 37 weeks of gestational age or less had a 1.5 crude odds ratio for developing pertussis versus those infants who were 38 weeks or greater.

Finally, in Table 7 the most significant predictor variables yielded after multivariate logistic regression and after adjustment using 10% odds ratio adjustment are listed. The seven significant predictor variables for pertussis were as follows: infant birth weight, infant birth type, maternal cigarette smoking, number of siblings living, paternal age, paternal education and paternal Hispanic origin.

Table 6

Crude Odds Ratios and 95% Confidence Intervals for Infant Characteristics

Variables	Cases n=451	Controls n=1353	Effect OR (95% CI)
Infant birth weight (grams)			
$\leq$1499	8	22	1.2 (0.5-2.7)
1500-2499	50	61	2.7 (1.8-3.9)
$\geq$2500	393	1270	Referent
Infant gestational age (weeks)			
$\leq$37	110	245	1.5 (1.2-1.9)
$\geq$38	327	1087	Referent
No. of siblings living			
0	146	526	Referent
1-4	290	787	1.3 (1.1-1.7)
$\geq$5	14	23	2.2 (1.4-4.4)

Table 6 (*continued*)

Variables	Cases n=451	Controls n=1353	Effect OR (95% CI)
Infant birth sequence			
1^{st}	426	1320	Referent
$\geq 2^{nd}$	25	33	2.3 (1.4-4.0)
Infant birth type			
Single	426	1320	Referent
Multiple (twins or more)	25	33	2.4 (1.4-4.0)
Infant sex			
Male	218	710	1.2 (0.9-1.5)
Female	233	643	Referent

Final analysis revealed six significant adjusted odds ratio variables greater than 2 remaining. After adjusting for confounding variables, the six most significant predictors were identified by order of strength as follows: a sibling number of 5 or greater (OR=3.1, 95% CI 1.4-7.2), paternal age less than or equal to 19 years of age (OR=2.9, 95% CI 1.7-5.1), paternal education level of high school graduate with some college (>12 and $\leq$15 years) (OR=2.4, 95% CI 1.5-3.8), birth weight between 1500 to 2499 grams (OR=2.2, 95% CI 1.3-3.7), a multiple birth type (born as part of a twin or triplet set) (OR=2.2, 95% CI 1.1-4.4) and mother's cigarette use (OR=2.1, 95% CI 1.3-3.5). One other variable, father's Hispanic origin (OR=1.5, 95% CI 1.1-2.0), followed in predictor significance although the respective odds ratio value was less than 2.

Table 7

Crude and Adjusted Odds Ratios of Significant Predictors for Pertussis

Variables	Cases n=451	Controls n=1353	Effect OR (95% CI)	Adjusted effect OR (95% CI)
Infant birth type				
Single	329	1097	Referent	Referent
Multiple	19	29	2.4 (1.4-4.0)	2.2 (1.1-4.4)
Infant birth weight (grams)				
<1499	8	22	1.2 (0.5-2.7)	1.5 (0.5-4.1)
1500-2499	41	66	2.7 (1.8-3.9)	2.2 (1.3-3.7)
≥2500	307	1060	Referent	Referent
No. of siblings living				
0	101	436	Referent	Referent
1-4	236	675	1.3 (1.1-1.7)	1.5 (1.2-2.0)
≥5	11	15	2.2 (1.4-4.4)	3.1 (1.4-7.2)
Does Mother smoke cigarettes?				
Yes	42	70	1.9 (1.3-2.8)	2.1 (1.3-3.5)
No	408	1341	Referent	Referent

Table 7 (*continued*)

Variables	Cases n=451	Controls n=1353	Effect OR (95% CI)	Adjusted effect OR (95% CI)
Paternal Age (years)				
≤19	39	59	2.5 (1.6-3.9)	2.9 (1.7-5.1)
20-29	182	557	1.2 (0.9-1.6)	1.2 (0.9-1.7)
30-39	123	462	Referent	Referent
≥40	19	97	0.7 (0.4-1.3)	0.9 (0.5-1.5)
Father Educational Level (years completed)				
≤8	33	111	2.1 (1.3-3.6)	1.3 (0.7-2.3)
>8 and ≤12	213	593	2.6 (1.8-3.7)	1.6 (1.0-2.4)
>12 and ≤15	62	153	2.9 (1.9-4.5)	2.4 (1.5-3.8)
≥16	41	296	Referent	Referent
Is Father of Hispanic origin?				
Yes	196	497	1.6 (1.3-2.1)	1.5 (1.1-2.0)
No	152	629	Referent	Referent

CHAPTER 4

DISCUSSION AND RECOMMENDATIONS

Discussion

After analysis was completed, seven variables were found to be significant predictors for pertussis in the data set. Of the original 16 variables selected for data analysis, the seven variables of significance were as follows: infant birth type, infant birth weight, number of siblings living, paternal age, paternal education level, paternal Hispanic origin and mother's cigarette use. All of these seven predictor variables had adjusted odds ratios greater than the value of 1. Six of the seven predictors produced significant adjusted odds ratios greater than the value of 2—siblings numbers of 5 or more, paternal age of 19 years and younger, paternal education level of high school graduate with some college (>12 and ≤15), birth weight level between 1500 to 2499 grams, multiple birth type and mother's cigarette use.

The greatest odds ratio value found among all variables was the number of siblings living. When comparing 0 siblings as the reference, a family size of 1 to 4 siblings had an odds ratio of 1.5 with a 95% confidence limit of 1.2 to 2.0. A sibling size greater than or equal to 5 tripled the odds of pertussis with a value of 3.1 with 95% confidence limits of 1.4 to 7.2. These results indicate new findings not previously found through other research; as the number of siblings increases, the odds of a household infant developing pertussis also increases.

While no current literature supports these exact findings, a previous study found similar results. The similar study uncovered a strong association between number of siblings and delay in pertussis immunizations (Reading, Surridge & Andamson, 2004). Reading (2004) found that as the number of older siblings increased, a delay in primary pertussis immunization increased for household infants and younger siblings. Two other studies found that infants from larger families were less likely to be fully immunized and more likely to have delayed immunization (Li & Taylor, 1993; Peckham, Bedford, Senturia & Ades, 1989). While the two studies did not specifically cover pertussis immunization, it illustrated that number of siblings affects timeliness of overall immunizations. This would create a vulnerable environment for infants with a large number of siblings.

Three more studies on immunization and birth order found similar results in that later born siblings were more likely to experience delayed immunization than firstborn children (Higgins, 1990; Kaplan, Mascie-Taylor & Boldsen, 1992; Schaffer & Szilagyi, 1995). This delay in immunizations as sibship (total number of children born to a set of parents) or as birth order increases may explain the findings in this study. Infants from households with large sibships and infants who are at a higher birth order may be at greater risk of developing pertussis infection because of the increased odds of intrafamilial contagion due to delay in immunizations.

As number of siblings was found to be of significant importance in this study, it would be worthwhile to further capture total household size information. Kaplan (1990) found that children born at higher birth order (later born children) index in larger households were more prone to infectious disease. On average, families with a higher birth order index child lived in crowded living situations with over three people per room. First and second born children lived in smaller households and experienced less crowding with an average of not more than one person per room. It can be reasonably surmised that as household size increases, chances for developing pertussis infection in infants increases. This may be due to closer proximities in sleeping arrangements with older siblings who may not be fully immunized. These older siblings may attend day care or school and be more prone to develop pertussis infection from ill classmates or fellow daycare attendees. Previous research has established that among infants for whom a source case was identified, household members were responsible for 76% to 83% of transmission of *Bordetella pertussis* to the infants (Wendelboe, et al., 2007). Infant siblings would be more susceptible to infection when in closer proximity to these siblings or household members who were infectious and actively coughing and sneezing. These findings further highlight the importance of vaccination in household contacts to infants.

In summary, number of siblings in a household may influence pertussis development in an infant due to delayed immunizations of infants or older siblings. Late immunizations may also be due to the relaxed nature of a seasoned parent who has been through immunization rounds with their first child. As numbers of siblings increase, overcrowding may also play a role in increasing opportunities for transmission of pertussis throughout households by putting infants in closer proximity to potential sources of exposure. Households with greater numbers of siblings may also face an economic barrier to routine and preventive medical care. A combination of all these factors may well be the reason number of siblings has an effect on pertussis development on infant households. Pertussis, when left untreated, can spread quickly throughout households.

Paternal age was the second variable of greatest significance found in this study. No current literature exists on paternal age and pertussis development, but previous research has found younger maternal age to be a predictor of pertussis development for infants (Izurieta et al., 1996). Perhaps a correlation exists between younger maternal age and younger paternal age, as it could be surmised that most adolescent parents would seek out a partner similar to their own age. This possibility would suggest that paternal age may influence pertussis development.

Two previous studies investigated the levels of maternal antibodies to pertussis (Gonik, Puder, Gonik & Kruger, 2005; Healy, Rench, Edwards & Baker, 2006). Both studies found that a large number of parous women had low or undetectable pertussis antibody levels, suggesting an increased susceptibility to infection and less of a chance for maternal transmission of effective antibodies through transplacental passage. Healy (2006) particularly found that Hispanic mothers of adolescent age had significantly lower levels of antibodies for pertussis than older mothers. Again, perhaps there is a correlation between maternal age and paternal age in regards to pertussis antibody levels. If younger mothers have less immunity to pertussis, maybe this is true for fathers as well. Younger adolescent fathers may not have yet developed antibodies to pertussis. These young fathers may not have been vaccinated and may not have developed proper antibodies that older fathers have in order to fight off pertussis infection. As discussed earlier, pertussis immunity may have waned in adolescent fathers who have not received booster vaccinations. Younger fathers who have little to no immunity to pertussis may be more prone to pertussis infection and in turn may spread the disease on to their infant child.

Special attention and instruction should be given to teenage fathers of infants. Younger fathers may be naïve to infection prevention and control practices. Adolescent fathers need to be educated on better hygiene practices including the importance of hand washing to prevent the spread of infection among households.

The third most significant predictor identified was paternal education level. Strangely, a paternal education level of high school diploma with some college (>12 and ≤15) yielded an odds ratio of 2.4 and a 95% confidence limit of 1.9 to 4.5 in comparison to college graduate fathers. In fact, as paternal education increased, odds for pertussis development in infants also increased. Fathers in the lowest education bracket yielded the lowest odds of infant pertussis development. Conventionally, it could be assumed that infants born to parents of a higher education level would face better odds of being healthier than infants born to parents of a lower education level. Because a higher education level is normally associated with a higher income, it could be assumed that as a parent's education level increased, their infant's odds for disease development would decrease because they were afforded better health care.

No current literature on paternal education and pertussis development exists, however, a similar effect on a child's overall vaccination level and higher maternal education level was identified in one study (Orenstein, Atkinson, Mason & Bernier, 1990) . This study examined barriers to vaccinating children and characterized the parents of those children. Two main groups of inadequately vaccinated children were identified; one group being undervaccinated (vaccinated, but not completely) and a second group of unvaccinated (never vaccinated) children. The first undervaccinated group was characterized as children who came from low-income, inner city households headed by young single Black mothers with less than high school education level. The second unvaccinated group was characterized as children who came from wealthier, suburban households (annual income > $75,000) where mother was White, married, older and college-educated (4-year degree or higher). This was one of the first studies to identify what is now a growing trend among more educated and affluent parents; a growing number of parents in the United States are now opting not to vaccinate their children.

In recent years, anti-vaccine sentiment has grown largely throughout the country. For different reasons, some parents are choosing not to vaccinate their children. While exemptions to vaccines have always existed due to religious objections or medical contraindications, a new group of vaccine exemptors is increasing. This new category of exemptors is commonly referred to as philosophical or conscientious exemptors. Philosophical exemptors in general believe that vaccines contain harmful byproducts and believe that risks outweigh the benefits. Many philosophical exemptors are similar in characteristic to the mothers identified in the earlier study as having unvaccinated children. Philosophical exemptor parents are often older, wealthier college-educated parents living in suburban neighborhoods. This may explain the surprising results of paternal education indicating higher risk for pertussis development in infants.

While the exemptor characteristic may help shed some light on paternal education level results, it still does not fully explain the reason for the increased odds of pertussis in higher education versus lower education levels. It is possible that there is some confounding within the resulted data that was not removed by the 10% adjustment method.

Low infant birth weight (1500-2499 grams) was the fourth significant variable identified. It makes biological sense that infant birth weight is a significant predictor of pertussis disease in infants. Infant birth weight is associated with the overall health of an infant. Infants born at a lower birth weight usually are born prematurely and may struggle with development and have weaker immune systems as a result of this. Pertussis literature has identified low infant birth weight with pertussis development. A study conducted in Ohio found that low birth weight infants were significantly more likely to have reported pertussis than normal birth weight infants (Langkamp & Davis, 1996). The study also found that low birth weight infants were also significantly more likely to be hospitalized with pertussis than were normal birth weight infants.

It also makes biological sense that infant birth type was selected out as the fifth significant predictor for pertussis disease in infants. With an odds ratio of 2.2 and a 95% confidence limit of 1.1 to 4.4, an infant born as part of a multiple birth set (twins or triplets) has twice the odds of developing pertussis versus an infant born in a single birth. This may be due to the fact that during multiple births, infants are sometimes delivered more prematurely than single births. Because of the premature delivery, an infant's immune development may be negatively impacted. Twin births often have discordant birth weights, with one twin being larger and overall healthier than the smaller twin sibling. Infant birth type has been identified in previous pertussis literature. One study examined twin births and found that discordant birth weights lead to mortality rates 11 times higher than non-discordant birth weights (Branum & Schoendorf, 2003).

Mother's cigarette use was the final variable found to be significant with an OR greater than 2 in this study. With an odds ratio value of 2.3 and a 95% confidence limit of 1.4 to 3.7, these results showed that infants with mothers who smoked cigarettes were twice as likely as infants whose mothers did not smoke to develop pertussis. These results indicate a new research finding not previously established by any other study; associating maternal smoking with increased odds of developing pertussis in infants. Past research has shown that maternal smoking increases the likelihood of respiratory infection in infants (Ahmer, et al., 1999; Ahmer, et al., 1998; Geng, Savage, Razani-Boroujerdi & Sopori, 1996; Saadi, et al., 1996; Stocks & Dezateux, 2003). Current and past research shows that maternal smoking especially during pregnancy has been associated with several adverse outcomes in infants. These outcomes include premature delivery, spontaneous abortion, growth restriction, increased risk of Sudden Infant Death Syndrome (SIDS), and long term behavioral and psychiatric disorders (Shea & Steiner, 2008). Another study found a significant association between maternal use of tobacco and the occurrence of postnatal infections in preterm neonates (Jeppesen, Nielsen, Ersboll & Valerius, 2008). Similarly, findings from this thesis project found maternal smoking increases odds of pertussis infection in infants. All of these research findings combined provide further supporting evidence establishing that maternal smoking is detrimental to an infant's health both during pregnancy and after birth.

Limitations of Study

This project would have had more power had one particular variable been chosen for analysis, such as paternal age. It is difficult to gauge the effects of many covariates with the statistical procedures that were used in this study alone. A more in depth project would have involved implementing Poisson regression to evaluate continuous variables and their effects on the outcome. The problem of multiple comparisons was also present in this study. A large data set was subjected to one outcome variable and with a large number of possible variables to choose from, there is an increasing likelihood that the acceptance criterion may have been satisfied purely by chance. Because there were differing data types, recoding to categorical variables seemed the better option for analysis. The outcome of this study may have been influenced by the recoding of continuous data. The elimination of variables due to missing data may also have impacted findings in this study.

A second possible limitation to this study is the use of birth certificate data to predict health outcomes. Literature on the use of birth certificate data has had mixed reviews. Some researchers have found the data to be useful for certain data elements and not for others. An earlier study on birth certificate use in Texas found serious validity and reliability problems (Northam & Knapp, 2006). Another study found that important descriptive data and outcome data for birth certificates were reliable while other uncommon events were not well noted (Zollinger, Przybylski & Gamache, 2005). With the implementation of an expanded birth certificate around the nation in 2003, birth certificate data are expected to provide more complete sources of information than current formats.

Lastly, a final limitation to this study may be the method for reporting pertussis disease. It is estimated that reported cases of pertussis represent only about 10% of actual cases since the 1940s because of disproportionate representation of classic and severe cases, bias towards reporting children, and a lack of uniform reporting for pertussis

(Castillo-Chavez, Blower & Van Den Driessche, 2002). Because passive surveillance is the main method used for gathering pertussis data in the state of Texas, there is the potential for bias such as those just mentioned in the previous reference.

Recommendations

It seems that there is still a common public misconception about pertussis being a rare disease, not often encountered in today's society. Public health officials and the medical community have a responsibility to increase public awareness and knowledge of the serious dangers of pertussis, especially to vulnerable infant populations. Specially targeted education campaigns for pertussis prevention in Texas need to include a focus on families with a large number of siblings, infants of young adolescent fathers, low birth weight infants, multiple births (twins or greater), and mothers of infants who smoke. Paternal education level needs further research before providing recommendation to use this variable to screen pertussis disease.

Households with large numbers of siblings including an infant less than 12 months of age need to be educated on the dangers of pertussis. Proper hand washing techniques and better hygiene practices need to be emphasized in order to prevent the spread of disease within these households. Also, parents of households with a large sibling base need to assure that all children, including older siblings and infants, are kept up to date on their immunizations.

While the booster vaccine for adolescents and adults is still fairly recent, it has demonstrated promising results thus far. Adolescent fathers as well as adolescent mothers of infants should also be immunized with the latest pertussis booster immunizations. Any regular visitors to the household who may have contact with an infant should be vaccinated. Adolescent parents of an infant should be educated on the signs and symptoms of pertussis and prevention methods. Further research into the association of paternal education level to pertussis disease development may be warranted. A comprehensive assessment on both maternal and paternal education level may also be worthwhile in order to evaluate any respective effects on pertussis development.

Enhanced smoking cessation programs in Texas are needed to target mothers who smoke. Physicians and other health care workers need to emphasize the importance of smoking cessation to pregnant mothers who smoke. Smoking cessation needs to begin as soon as a mother knows she is pregnant. Any other smoking family members also need to be educated on the dangers of second hand smoke in relation to infants. Smoking in households needs to be avoided after the birth of an infant.

Overall, Texas birth certificate data was found to be a useful tool for identifying predictors of pertussis disease in infants. Further research may be warranted on households with a large sibship, young paternal age, paternal education levels, infant birth weight, infant birth type and maternal smoking to assess their respective influence on pertussis risk in infants. The establishment of significant predictors would aid public health officials in identifying pockets of need throughout the community. Consequently, the establishment of predictors would provide support for more funding and focus in these populations to help reduce the spread of pertussis.

APPENDIX

TEXAS DEPARTMENT OF STATE HEALTH SERVICES

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February 29, 2008

Lucille Palenapa
Infectious Disease Control Unit
Department of State Health Services
1100 W 49th St - MC 1939
Austin, TX 78756-3199

Research - Expedited Review Approval Identifying Risk Factors for Pertussiss in Infants Less Than 12 Months of Age in Texas Utilizing 1999-2004 Surveillance and Birth Certificate Data, IRB# 06-088

Dear Ms Palenapa

Upon review of your submission for the above-referenced project, the Department of State Health Services Institutional Review Board #1 (IRB) determined that the project could be approved using an expedited review process based on the Code of Federal Regulations 45 CFR 46 110(b)(1), category 8C

The approval will expire on 12/20/2008. You will need to apply for an extension *before* the approval expires if your project will continue beyond that date

Under federal rules and DSHS procedures, the principal investigator of your project is responsible for

a Submitting for IRB review any modification to the protocol or consent forms prior to the implementation of the change, except when necessary to eliminate *apparent immediate hazards* to the subject, after which the modification must be reported,
b Protecting the confidentiality of all personally identifiable information collected and training your staff and collaborators on policies and procedures for ensuring the confidentiality of all such information,
c Applying for renewal by the IRB at least two months before the expiration of this approval,
d Informing the IRB if the project will conclude on or before the expiration date by visiting our website, downloading and completing the Final Report upon Termination of Project form, and submitting it before the expiration date You may fax a copy of the Final Report form to (512) 458-7344, and
e Notifying the IRB immediately of any occurrences of adverse events related to this project

If you have questions, please contact the IRB Administrator, Steven Lowenstein, at (512) 458-7111, extension 2202 or toll-free at 1-888-777-5037, or by e-mail at steven lowenstein@dshs state tx us You may also visit our website at www dshs state tx us/irb

In any future correspondence concerning this project, please reference the IRB tracking number noted above

Sincerely,

John F Villanacci, Ph D , NREMTI
Chair, DSHS Institutional Review Board #1
FWA00008616/IRB00004733

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cc file (06-088)

TEXAS DEPARTMENT OF STATE HEALTH SERVICES

CHARLES E BELL, M D
ACTING COMMISSIONER

1100 W 49th Street • Austin, Texas 78756
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TDD 512-458-7708

Dr Ram Shanmugam, Associate Professor & Ms. Lucille Palenapa, Graduate Student
Department of State Health Services Research
Texas State University
601 University Drive
San Marcos, Texas 78666-4616

Dear Ms. Palenapa and Dr Shanmugam

Ms Lucille Palenapa, graduate student in the Health Services Research Program at Texas State University, has requested permission to use data from the Texas Department of Health (TDH) Infectious Disease Control Unit (IDCU) for her master's thesis She has indicated that Dr. Shanmugam will serve as chair for her thesis committee I approve of her proposal to study "Identifying Predictors for Pertussis Disease in Infants Less than 12 Months of Age in Texas Using Surveillance Records and Birth Certificate Data for Infants from 1999-2004 "

I grant both of you permission to use the data from the case-control component for the purpose of Ms Palenapa's thesis project. You are permitted access to data that has been specifically abstracted and has had all personal identifiers removed for the purpose of this study

If you need any additional information, please feel free to contact me at 512-458-7676.

Sincerely,

Kaye Shields, Data Manager
Infectious Disease Control Unit

CDC Case Definition for Pertussis (Whooping Cough)

Clinical Case Definition

A cough illness lasting at least 2 weeks with one of the following: paroxysms of coughing, inspiratory "whoop," or post-tussive vomiting without other apparent cause (as reported by a health professional).

Laboratory Criteria for Diagnosis

- Isolation of *Bordetella pertussis* clinical specimen
- Positive polymerase chain reaction (PCR) for *B.pertussis*

Case Classificiation

Probable: meets the clinical case definition, is not laboratory confirmed, and is not epidemiologically linked to a laboratory-confirmed case

Confirmed: a case that is a culture positive and which an acute illness of any duration is present; or a case that meets the clinical definition and is epidemiologically linked directly to a case confirmed by either culture or PCR

Comment

The clinical case definition above is appropriate for endemic or sporadic cases. In outbreak settings, a case may be defined as a cough illness lasting at least 2 weeks (as reported by a health professional). Because direct fluorescent antibody testing of nasopharyngeal secretions has been demonstrated in some studies to have low sensitivity and variable specificity, such testing should not be relied on as a criterion for laboratory confirmation. Serologic testing for pertussis is available in some areas but is not standardized and, therefore, should not be relied on as a criterion for laboratory confirmation.

Both probable and confirmed cases should be reported nationally.

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VITA

Lucille Leilua Palenapa was born in Fort Riley, Kansas on August 13, 1977, daughter of Petesio and Maria Palenapa. She attended Denbigh High School in Newport News, Virginia; Faasao High School in Lepuapua, American Samoa; Samoana High School in Utulei, American Samoa; Killeen High School and finally graduated from Ellison High School in Killeen, Texas. She graduated with a Bachelor of Science degree in Community Health from Texas A&M University in College Station, Texas in August 2000. She currently works in the Infectious Disease Control Unit of the Texas Department of State Health Services with a primary focus on vaccine-preventable diseases. She entered the Graduate College of Texas State University-San Marcos in September of 2004.

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