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Maternal Characteristics and the Risk of Cleft Lip and Palate in the United States

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Abstract

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by

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MSN, University of Manchester, 2004

BSN, Armed Forces Medical College, Pune University, 1989

Dissertation Submitted in Partial Fulfillment

of the Requirements for the Degree of

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Abstract

Cleft lip with or without cleft palate (CLP) is an ongoing public health issue across the globe, and in the United States. The estimated number of babies born each year in the United States with cleft palate (CP) is about 2,650, while CLP affects approximately 4,440 babies. The purpose of this quantitative cross-sectional study was to determine if there is a relationship between CLP and maternal characteristics such as reproductive history (advanced maternal age, maternal obesity, prenatal visits, month prenatal care began, number of pregnancies, gestational age at birth, assisted reproductive technology used, gestational diabetes, and hypertension), socioeconomic status of the mother (marital status, education, mother's race, payment source for delivery, and place where birth occurred), and admission to the Neonatal Intensive Care Unit (NICU) in U.S. hospitals from January 2016 to December 2016. The epidemiological triad theory served as the study's framework. A secondary dataset from the National Vital Statistics System was used for this study. Logistic regression was used to test the hypothesized associations. Results indicated that many maternal characteristics such as mother's age (p = .000), maternal obesity (p = .020), number of prenatal visits (p = .001), total birth order (p = .001), gestational age at birth (p = .000), gestational diabetes (p = .002), and gestational hypertension (p = .032), mother's education (p = .000), marital status (p = .018), race (p = .000), and admission to NICU (p = .000) were significantly associated with CLP. Results of this study may help health care professionals identify the determinants of the risk of CLP so as to design and implement effective CLP preventive measures among United States populations that are disproportionately affected by this condition.

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Dedication

I dedicate this dissertation to my husband Thomas Eapen for taking this journey with me, supporting my efforts, and encouraging me all the way. I thank you for your patience, continued support and encouragement and for taking over a big portion of chores in the house. This is also dedicated to my children, Angela Thomas, Alan Thomas and Aleysha Thomas for your support and understanding, especially when I could not give you my undivided attention due to studying and researching; you guys are simply the best. I thank you for believing in me, for your encouragement, positive attitude and finally for just being there for me. I love you all! Pursuing a doctoral degree was a challenge in my life, and I could not have done it without your help. Thank you again!

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Chapter 1: Introduction to the Study

Introduction

In the United States, approximately one in 33 births are diagnosed with birth defects (Ramakrishna, 2013). Those ranking amongst the most common include neural tube defects, Down syndrome, and orofacial clefts, which include cleft lip (CL), cleft lip with cleft palate (CLP), and cleft palate alone (CP) (World Health Organization [WHO], 2010). Oral clefts are considered one of the prominent causes of infant mortality in the United States. Due to both environmental and genetic factors, CP rates differ across geographic regions and within ethnic groups, but the WHO estimates that one out of every 500 to 700 live-births involve a cleft of the lip or palate, making it one of the most common birth defects not only in the U.S. but across the globe (Kutbi, 2014). Of all forms of birth defects, orofacial cleft is the second most common in the United States, with a prevalence of 10.63 per 10,000 live births. This equates to one in every 940 births, resulting in 4,437 cases every year (Parker et al., 2010). Unfortunately, developing countries with populations of low socioeconomic status seem to suffer most from increased risk of CL and CP (Kutbi, 2014). However, despite its expansive prevalence, researchers have yet to clearly identify the potential causes and risk factors of CLP.

The causes of CLP appear to intersect across a wide-range of categories from maternal and prenatal to environmental. Identified maternal risk factors include maternal demographics, biological factors, and maternal habits of smoking and alcohol use. However, factors such as chromosomal disorders, gene defects, environmental pollution, and micronutrient deficiencies are also identified as causes of CLP (WHO, 2010).

Additionally, the WHO (2010) has found that maternal infectious diseases such as syphilis and rubella are a concern for birth defects along with other maternal risk factors including diabetes mellitus, deficiency of folic acid, use of medicinal and recreational drugs, exposure to certain chemicals in the environment, and high doses of radiation.

Due to many factors such as population sample, surveillance methodology, and clinical classifications, proper epidemiological estimates of orofacial clefts vary substantially (International Perinatal Database of Typical Oral Clefts Working Group, [IPDTOC], 2011). Despite this variance, its prevalence is evident under its umbrella classification of all orofacial deformities. According to the WHO (2001), this classification includes CLP in any form (CL, CP, and CLP), which occurs in one out of every 700 live births. Worldwide estimates of CL with or without CP range from 7.94 to 9.92 per 10,000 live births (IPDTOC, 2011; Tanaka, Mahabir, Jupiter, & Menezes, 2012). Isolated CP is less frequent, presenting in only one out of every 1,574 births (Parker et al., 2010).

The occurrence of orofacial clefts varies by population. Overall, higher rates have been reported in Asians and American Indians (one in 500 births), while lower rates have been reported in African-derived people (one in 2,500 births; Dixon, Marazita, Beaty, & Murray, 2011). As for the United States, a recent report from the Centers for Disease Control and Prevention (CDC, 2016) showed that about 2,650 babies are born with a CP, and about 4,440 babies are born with a CL with or without a CP each year. Isolated orofacial clefts (clefts with no other significant congenital disabilities) are one of the most common types of birth defects in the United States. Depending on the cleft type, the rate of isolated orofacial clefts varies from 50% to 80% of all clefts (Little, Cardy, & Munger, 2004; Honein et al., 2007; Yazdy, Autry, Honein, & Frias, 2008).

Considering the vast range of risk factors and the environmental factors for CLP, I deemed it necessary to conduct a study focused on identifying the underlying risk factors that cause CLP. My goal was to analyze various potential independent variables in hopes of producing results that future researchers could interpret these findings as significant information to identify and confirm possible underlying risk factors of CLP. Healthcare professionals can leverage the findings to implement more effective preventative efforts and better identify risk factors at earlier stages of prenatal care. These efforts could include using insights from my study to educate women of potential risk factors, which could stimulate social change amongst at-risk women to avoid related prenatal behavior and encourage them to improve their pregnancy care to develop a healthier baby. Healthcare professionals could also better identify risk factors at earlier stages of prenatal care, resulting in the prevention of further adverse effects.

In Chapter one, I provide background on CLP and discuss the purpose of the study, research questions, theoretical framework of the study, and the nature of the study. Next, I provide operational definitions of fundamental concepts in this research and present the study's assumptions, limitations, scope and delimitations. Finally, I discuss the significance of the study and provide a summary.

Background

CLP is the second most common congenital anomaly in the United States, presenting approximately 7,000 new cases annually (Parker et al., 2010). CLP or CL alone is a closure deformity that is developmental defect, involving the improper fusion of the palatal shelves or the nasal process (Olasoji, Ukiri, &Yahaya, 2005). Among the orofacial defect population, the most common diagnosis is CLP (46%), followed by isolated CP (33%) and then isolated CL (21%). The majority of bilateral CL (86%) and unilateral CL (68%) are associated with a CP (Hopper, Cutting, & Grayson, 2007). Unilateral clefts are nine times as common as bilateral clefts and occur twice as frequently on the left side than on the right.

The occurrence of CL with or without palate seems to differ across racial lines. In the White population, CL with or without CP occurs in approximately one in 1,000 live births (Hopper, Cutting, & Grayson, 2007). These entities are twice as common in the Asian community, and almost half as prevalent in African Americans (Hopper et al., 2007). However, this racial heterogeneity is not observed for the isolated CP, which has an overall incidence of 0.5 per 1,000 live births (Hopper et al., 2007). In the White population, the prevalence is 1 to 1.5 out of 1,000 live births; in African and African-American communities, the prevalence is less than 0.5 out of 1,000 live births; and in Asian and Hispanic populations, isolated CP occurs in two to three of every 1,000 live births (Das, Runnels, Smith, & Cohly, 1995).

Orofacial clefts and their occurrences also correlate with family history and heritage. Parents without clefts who have already had one child with a CL or CP have a 5% chance of having another child with a CLP compared to the usual 0.14% risk in parents with no family history of cleft (Hopper et al., 2007). If both a parent and a child have a cleft, or if two normal parents have two children with clefts, the likelihood of a cleft occurrence in another child increases to 15–20%. These data seem to suggest a genetic component; however, the development of CL/CP is probably due to a combination of factors such as folic acid deficiency, advanced maternal and paternal age, use of anticonvulsants (phenytoin or phenobarbital), alcohol intake, and possibly smoking. Some researchers also suggest a viral etiology for CLP (Hopper et al., 2007; Lip, 2015).

CL and CP are often found in association with other genetic syndromes, including velocardiofacial syndrome and Van der Woude syndrome (Cohen, 1978; Venkatesh, 2009). Classified as "syndromic," these patients can display a variety of deformities that range from mild to severe. Non-syndromic clefts, however, are more common and have been estimated to represent 50% to 70% of all orofacial clefts (Calzolari et al., 2007; CDC, 2015; Jones, 1988; Tolarova & Cervenka, 1998). A combination of genetic and other factors may cause orofacial clefts, such as environmental exposure, maternal diet, smoking, and medication use (CDC, 2015; Dixon et al., 2011; Honein et al., 2007).

A study conducted by Marazita et al. (2004) also showed a genetic association for CLP. In result, parents who have a child with a non-syndromic cleft, or a family history of clefting often ask about their risk of clefts in subsequent pregnancies (Hopper, Cutting, & Grayson, 2007). Both environmental teratogens and genetic factors are implicated in the genesis of CLP (Murray, 2002). Mothers who use tobacco during pregnancy increase the incidence of having a baby with a CLP status (Honein et al., 2007). Other teratogens, such as alcohol, anticonvulsants, and retinoic acid are associated with congenital malformation that include CLP but have not been directly related to isolated CP cases

(Hopper et al., 2007). CLP syndromes may also be due to genetic abnormalities that include clefts of the primary or secondary palates among the affected developmental fields. Malformation syndrome is usually part of more than 40% of CLP, compared to less than 15% of CL and CP cases (Hopper et al., 2007).

Treatment of orofacial clefts consist of surgical intervention to correct anatomy and function (Robin et al., 2006). Surgical repairs facilitate normal facial development, and thus improve multiple outcomes, including speech and language development, dental formation, and psychosocial issues (Cassell et al., 2009). For CL, CP, and CLP, a timely completion of the initial primary surgery is essential to allow for proper development. The American Cleft Palate-Craniofacial Association (ACPA) recommends that primary surgical repair of CL occur within the first 12 months of life and may be performed as early as is considered safe for the infant. For CP, the ACPA recommends primary surgery by the age of 18 months and earlier, if possible (ACPA, 2009; Thompson, Heaton, Kelton, & Sitzman, 2017).

Individuals born with CL, CP or both require coordinated care from multiple specialties to optimize treatment outcomes. The ideal care is in a center with a multidisciplinary cleft team dedicated to treating cleft-related issues from birth to adulthood (Hopper et al., 2007). Typical members of a cleft team include an audiologist, dentist, geneticist, nurse, nutritionist or dietitian, oral surgeon, orthodontist, otolaryngologist, pediatrician, plastic surgeon, psychologist, social worker, and speech pathologist. A cleft team places more emphasis on coordination of care to minimize the number of surgeries performed while maximizing the benefit to the patient. Although the number of surgical procedures required before adulthood has decreased with improved techniques, care of a child with a cleft still requires a complicated and lengthy surgical treatment plan. A cleft team's goal is to eliminate as many steps in the treatment plan as possible, thereby optimizing the outcome and benefit of each essential intervention (Hopper et al., 2007).

However, other researchers have indicated the possibility of prevention by revealing maternal risk factors ranging from prenatal behavior to environmental situations. Angulo-Castro et al. (2017) conducted a study among a Mexican population that linked maternal risk factors such as smoking, alcohol abuse, and a patient's neglected intake of folic acid and multivitamins during pregnancy to the development of CL and CP. Meanwhile, research conducted by Chincharadze, Vadachkoria, and Mchedlishvili (2017) showed that other risk factors such as contracting infectious or non-communicable diseases during the first trimester of pregnancy, as well as the use of medications, have some impact on the development of these malformations. However, Chincharadze et al. identified stressful situations in the families of the pregnant women as one of the most significant factors in the development of CLP.

Nagalo, Ouédraogo, Laberge, Caouette-Laberge, and Turgeon (2017) showed that medical conditions such as anemia, infections, malnutrition, and medical co-morbidities have a direct impact on congenital malformations in children with orofacial clefts in western Africa. Nagalo et al. (2017) concluded that further research is required and recommend having a National Malformations Registry to improve clinical understanding of OFC's. Pons-Bonals, Pons-Bonals, Hidalgo-Martínez, and Sosa-Ferreyra (2017) indicated the need to standardize the data registration on medical records to improve the monitoring and treatment of patients and emphasize actions to maintain a low incidence of CLP. Pons-Bonals et al. (2017) aimed to generate the clinical-epidemiological profile of CLP patients from a hospital in Mexico. The variables studied included those of the mother's pregnancy such as the patient's health at birth, nutrition, and psychomotor development. Other variables included family medical history, addictions, socioeconomic factors, and clinical profiles of the treated population registered. Pons-Bonals et al. interpreted their results as support for the need to standardize the data registration on medical records to improve the monitoring and treatment of patients and emphasize actions to maintain the low incidence of CLP (Pons-Bonals et al., 2017).

Wehby et al. (2017) suggested that oral clefts are associated with maternal smoking and are most common among underweight mothers, although the smoking-BMI interaction is strongest for CL and CP only. Ozturk et al. (2015) found that exposure to nicotine during pregnancy inhibits healthy fetal growth and development, resulting in persistent midline epithelial seam with the formation of type B and C patterns of palatal fusion. Shibui et al. (2016) discussed advancements in technology that have enabled prenatal diagnosis of CLP as well as the imperative to provide parents with mental care after diagnosis of CLP based on ultrasonography. The researchers discussed diagnoses, treatment process, and prenatal counseling provided to reassure parents that postnatal support would be provided from the start.

However, despite information gleaned by several researchers on the etiological factors of CLP, further research is still required to properly identify and confirm risk factors for CLP. There is no recently conducted study in the United States to determine the risk factors, thus there remains a gap in recent literature regarding the factors contributing to the status of CLP in the United States. Identifying these factors is critical to the potential implementation of prevention programs to reduce the incidence of CLP in the U.S. population. Meanwhile, the financial burden has climbed in the recent years due to increased admissions to Neonatal Intensive Care Unit (NICU) and other needs for children affected with CLP. Therefore, this study was needed to bridge the gap in knowledge regarding CLP and underlying risk factors among the United States population.

Problem Statement

Congenital disabilities are a chief cause of infant mortality in the United States, and about one in 33 infants are diagnosed with such birth defects (Ramakrishnan, 2013). Among those birth defects, craniofacial anomalies, which include CLP, have a global incidence of one in 700 live births with associated psychosocial and clinical effects (Olasoji et al., 2005). Isolated orofacial anomalies or clefts without other significant anomalies have the highest incidence of birth defects in the United States (Parker et al., 2010). The impact of orofacial clefts ranges from 50% to 80% of all clefts depending on its type (Little et al., 2004; Yazdy et al., 2008). The estimated number of babies born each year in the United States with cleft palate is about 2,650, and those born with CL with or without a CP are approximately 4,440 (Parker et al.,2010). The WHO estimates that one out of every 500 to 700 live births involve a CL or CP, making these defects a common issue worldwide (Kutbi, 2014).

CLP is a significant birth defect that presents a wide variety of medical, financial, and psychosocial burdens for the afflicted patient and their families. Based on both environmental and genetic factors, CLP rates differ across geographic regions and within ethnic groups— unfortunately, CLP most significantly affects those in developing countries where populations of low socioeconomic status and thus would be least capable to handle the associated burdens and financial impacts from CLP (Kutbi, 2014).

Although other birth defects and CLP can be considered common, its etiological background has not been precisely identified. Possible causes of birth defects include a vast array of maternal risk factors including maternal demographics (lower educational levels, lower income levels, and biological factors) and maternal behaviors such as cigarette smoking and excess alcohol use (Wu et al., 2007). In addition, a plethora of other risk factors are correlated with birth defects. Various studies from the WHO have shown several risk factors for birth defects: chromosomal disorders, gene defects, environmental pollution, and micronutrient deficiencies are some of the most significant factors (WHO, 2010). Additionally, other maternal factors include diabetes mellitus, deficiency of folic acid, medicinal and recreational drug exposure, exposure to certain chemicals in the environment, and high doses of radiation (WHO, 2010). Studies in developmental biology have shown that genetic and environmental factors are also thought to be involved in etiology of oral clefts (Olasoji et al., 2005). However, without knowing the precise etiology, proper care for oral clefts cannot be optimal and the prevention of oral clefts is not possible.

A recent study conducted in China on maternal risk factors and adverse birth outcomes indicated a strong correlation between different maternal characteristics and risk factors that result in CLP (Zheng, 2012). Several maternal factors influence the reduction and prevention of such birth outcomes across the world (Zheng, 2012). Women’s levels of income and education affect birth outcomes as well. Studies have shown that there is a close association between orofacial defects and advanced maternal age at delivery, lower maternal education, lower household income, higher alcohol consumption before and during pregnancy, smoking, obesity, and assisted reproduction (Osmond & Barker, 2000).

But despite an increased understanding of disease etiology in recent years, CLP abnormalities continue to be a burden on society (Boyle et al., 2011). Although many researchers have studied CLP on specific maternal behaviors across the world, there is a significant lack of recent research on CLP and its association with several maternal predisposing factors such as maternal behaviors, reproductive history, and the use of assisted reproductive technology among women in the United States (Cervantes, Keith, & Wyshak, 1999). Moreover, the financial burden due to increased admission to the NICU has increased in the recent years. High rates of CLP among the population are indicative of a lower quality of health care and decrease in the well-being of the population. A significant gap in the literature remains regarding the various risk factors for adverse pregnancy outcomes, which in turn impedes upon healthcare professionals’ ability to conduct effective prevention programs and education of CLP. This gap made it imperative that I conduct a study investigating these various risk factors for CLP to identify and eventually implement more effective programs to prevent the occurrence of CLP based on which risk factors are precisely associated with these birth defects.

Purpose of the Study

The purpose of this quantitative, descriptive, non-experimental study was to determine if there is a relationship between CLP and potential maternal risk factors such as maternal reproductive history (advanced maternal age, maternal obesity, number of prenatal visits, month prenatal care began, number of pregnancies, gestational age at birth, assisted reproductive technology used, gestational diabetes, and gestational hypertension), socioeconomic status of the mother (marital status, education, mother's race, payment source for delivery, and place where birth occurred) and admission to the NICU in U.S. hospitals from January 2016 to December 2016.

Research Questions and Hypotheses

RQ1: Is there a significant relationship between CLP and maternal reproductive history (advanced maternal age, maternal obesity, number of prenatal visits, month prenatal care began, number of pregnancies, gestational age at birth, assisted reproductive technology used, gestational diabetes and gestational hypertension) among mothers who delivered live infants in U.S. hospitals and birthing centers from January 2016 to December 2016?

$H_0$1: There is no significant relationship with CLP and maternal reproductive history (advanced maternal age, maternal obesity, number of prenatal visits, month prenatal care began, number of pregnancies, gestational age at birth, assisted reproductive technology used, gestational diabetes, and gestational hypertension) among mothers who delivered live infants in U.S. hospitals and birthing centers from January 2016 to December 2016.

$H_1$1: There is a significant relationship with CLP and maternal reproductive history (advanced maternal age, maternal obesity, number of prenatal visits, month prenatal care began, number of pregnancies, gestational age at birth, assisted reproductive technology used, gestational diabetes, and gestational hypertension) among mothers who delivered live infants in U.S. hospitals and birthing centers from January 2016 to December 2016.

RQ2: Is there a significant relationship between socio economic status of the mother (marital status, education, and mother's race, payment source for delivery, and place where birth occurred) and CLP resulting in admission to the NICU in U.S. hospitals from January 2016 to December 2016?

$H_0$2: There is no significant relationship between socioeconomic status of the mother (marital status, education, and mother's race, payment source for delivery, and place where birth occurred) and CLP resulting in admission to the NICU in U.S. hospitals from January 2016 to December 2016?

$H_1$2: There is a significant relationship between socioeconomic status of the mother (marital status, education, and mother's race, payment source for delivery, and place where birth occurred) and CLP resulting in admission to the NICU in U.S. hospitals from January 2016 to December 2016?

Theoretical Framework for the Study

I used the epidemiological triad theory to describe the potential causes of CLP among infants. Stevens first published the epidemiological disease triangle theory in 1960, although the interaction among plant, pathogen, and environment was certainly recognized earlier by plant pathologists (Stevens, 1960). For example, Duggar wrote in 1909 that "the abundance of a very large number of fungous [sic] diseases is directly connected with or conditioned by climatological factors . . . factors may affect independently, host and parasite, and they may affect the interrelations of these organisms" (Duggar, 1909, p.1). The theory is a traditional model that CDC researchers have used to increase knowledge on health difficulties (CDC, 2009). In the past, CDC scientists have used this model as a framework or method to prevent communicable disease (CDC, 2009; Russell, 2010; Nies & McEwen, 2007). Epidemiologists have used the theory in the past to explain prevalence of infectious disease and mental illnesses (Kebede, 2004; Russell, 2010). According to this theory, the epidemiological triad entails the agent, mode of transmission, and host (Dicker, 2008). According to the epidemiological triad model, a disease is transmitted only once the agent leaves its host through a portal of exit, and is transported via the mode of transmission through an appropriate gateway to infect a vulnerable host (Dicker, 2008). This type of communication can be direct or indirect. Directly, the immediate transmission occurs through direct contact (host-to-host). Indirectly, various means such as suspended air particles, inert objects (fomites), or living mediators (vectors) can transfer the infectious agent from the reservoir to the susceptible host.

According to this model, the causal agent is the causative factor for the disease (Dicker, 2008). In my study, these factors include maternal demographics, biological factors, maternal obesity, tobacco use, and maternal assisted reproduction. The reservoir houses the agent. Mode of transmission is defined as the process by which the agent is being transferred to its host, using either direct or indirect communication, or through a vector-borne method (Dicker, 2008). In this study, the mode of transmission occurs through the placenta through which etiologic agents are passed to the newborn. The causal agents are transferred to the baby through direct means (such as maternal smoking of tobacco products or maternal alcohol intake), indirect methods (maternal demographics or maternal prenatal care), or through a vector-borne method (sick mother). Last, in the epidemiological triad, the host is the infant since the birth outcome is influenced by mother's decisions and behaviors (Brown, 2011).

Nature of the Study

I used a quantitative and cross-sectional design to determine the relationship between maternal characteristics and CLP. The quantitative method was appropriate for the study because the secondary data I obtained were mostly statistical in nature and the results of this research was analyzed using mathematically based methods (see Aliaga, & Gunderson, 2002). I used a cross-sectional analysis to assess the relationship between maternal characteristics, demographics, and risk factors such as diabetes, assisted reproduction, obesity, and other infections for CLP. The dependent variable for the study was the existence of CLP. The independent variables included maternal reproductive history (advanced maternal age, maternal obesity, number of prenatal visits, month prenatal care began, number of pregnancies, gestational age at birth, earlier babies with congenital anomalies, use of assisted reproductive technology, gestational diabetes, and gestational hypertension), low socioeconomic status of the mother (marital status, education, and mother's race, payment source for delivery, and place where birth occurred), and CLP resulting in admission to the NICU (indicating high health care cost). For data analysis, I used both descriptive and logistic regression analysis to identify the risk factors and the relationship between variables. The purpose of using logistic regression in this research was to determine the association of CLP with the selected variables.

Secondary data for this study came from the publicly available birth data registry from the CDC National Center for Health Statistics (NCHS) records. Data abstraction involved extracting the data from the U.S. birth certificates records. The data base contained birth data collected in 50 states of United States during January 2016 to December 2016 (CDC, 2016). This publicly available dataset contains records of all births to United States residents and non-residents. I conducted a descriptive statistical analysis using the software, Statistical Program for Social Sciences (SPSS).

Definitions of Terms

Cleft lip and palate (CLP): CL and CP are facial and oral malformations that occur during pregnancy when a baby's lip or mouth does not form properly. These birth defects together are called "orofacial clefts" (CDC, 2017). A cleft lip occurs when the tissue that makes up the lip does not join completely before birth resulting in an opening in the upper lip. A cleft palate happens when the tissue that makes up the roof of the mouth does not completely join during pregnancy (CDC, 2017).

Live birth: Live birth refers to the complete expulsion or extraction of an infant from its mother as a product of human conception, irrespective of the duration of pregnancy, which breathes or shows any other evidence of life, such as beating of the heart, pulsation of the umbilical cord, or definite movement of voluntary muscles (NCHS), 2016).

Live birth order and parity: Live birth order and parity classifications refer to the total number of live births the mother has had including the 2016 birth. Fetal deaths are excluded. Live birth order indicates what number the present birth represents (NCHS, 2016).

Estimated gestational age: Gestational age refers to physician's estimate of gestation of the pregnancy in number of weeks (NCHS, 2016).

Prenatal visits: The independent variable prenatal care visits refers to the number of times during her pregnancy a mother sought health services related to her pregnancy and impending birth, reported in the birth data (NCHS, 2016).

Assumptions

During the study, I made a few assumptions. In regard to data quality, I assumed that the data collected from 2016 birth certificate data were accurate, since they were collected by the CDC. However, the data were self-reported. The validity risk for self-reported data may be affected by the fear of reprisal. The data I used can be considered reliable because the CDC is known to have reliable instruments and well-planned methodologies for data collection. Furthermore, the data were not collected for a specific defined outcome, allowing it to remain both versatile and objective. After consideration of these factors, I assumed the data to be of high quality.

I assumed that the study sample was representative of the total number of expectant women living in the United States who gave birth to live infants in hospitals and birthing centers from January 2016 through December 2016. Only births occurring to expectant women living in the United States were included. I also assumed that the results and reports of the study would be generalizable for the entire U.S. population.

The birth data leveraged in this study derived from the CDC’s data repository for epidemiologic research known as Wide-Ranging Online Data for Epidemiologic Research (WONDER). Wonder is an easy-to-use, menu-driven system that provides access to a wide array of public health information resources from the CDC. It is available to public health professionals and the public at large. All birth certificate data included in WONDER conform to the reporting criteria of the mother's place of residence, rather than the actual standards on the birth certificate issued by the reporting area of occurrence (NCHS, 2016). .

Also, there was a high chance of overlooking and underestimating some of the factors that may have contributed to CLP among residents who may not have been represented in the sample data. However, according to a report from the MacDorman, Mathews, and Declercq (2012), 99% of women in the United States give birth in hospitals. Therefore, I assumed that this had a minimal effect on the results because the portion of the population who are not represented in the study seems to be minimal. Although the effect is minimal, this fact was still counted towards the study population. Finally, I assumed that the framework fits with the epidemiological theory— that is, I assumed that a mother's behaviors during pregnancy can be the cause of CLP among infants.

Scope and Delimitations

Births occurring to U.S. citizens or residents outside of the United States are not included in the WONDER Natality file. The study population was limited to women of childbearing age in the United States. Data from live births occurring to U.S. citizens or residents outside the United States were not collected. The 2016 final birth report marks the first year in which data for all 50 states and the District of Columbia (D.C.) were collected. These are based on the 2003 revision of the U.S. Standard Certificate of Live Births in United States. Natality data are limited to births occurring within the United States, including those occurring to U.S. residents and nonresidents (NCHS, 2016). I also limited the study to certain specific risk factors that affected the CLP incidence in United States residents. I explored the relationship between these variables and CLP using data gathered from January to December 2016. The covariates included maternal reproductive history and low socioeconomic status of the mother that lead to increased rate of admission to the NICU indicating a high cost.

For this study, I selected specific maternal characteristics for several reasons. First, understanding current risk factors may aid in creating CLP prevention programs that are targeted to these specific risk factors among high risk populations. In addition, these factors were among the most prevalent factors in the literature concerning CLP, while several others were not addressed as contributing factors among Unites States population. Finally, a study of these factors may be of use to local or state agencies working to create CLP prevention programs.

There are approximately 327 variables available in the birth certificate Natality data set. I did not use some of those variables such as other infections, delivery mode, complications during delivery, and infant's father's details. I omitted these variables because, in regard to prevention amongst the targeted population, their data may not be considered relevant. I delimited the study to U.S. residents who gave birth to live infants in any hospital or birthing center between January 1, 2016 and December 31, 2016, as recorded in the Natality data set. The Natality dataset also excluded women who gave birth to live infants outside of a Unites States hospital or a birthing center. The research study also excluded data from those women who gave birth to live infants, but for whom there is absence of a complete birth record.

I used the epidemiological theory as the framework for this study. This theory provided sufficient structure to understand maternal behaviors and other maternal characteristics. I determined that this theory would be effective for my goal of providing insight on how mothers can make better choices concerning behavior, lifestyle, and prenatal care during their pregnancy. Understanding these different behavioral decisions and their consequences is crucial for developing and implementing population specific prevention programs among targeted women in the United States.

Although the epidemiological theory is a valid theory for the prevention strategies, another potential choice was to use the health belief model (HBM) as a conceptual framework for the study. The health belief model became one of the most extensively accepted conceptual outlines of health behavior that focuses on individual behavioral changes and identifying the relations of health behaviors, practices and utilization of health services (Green & Murphy, 2014). However, this theory was not effective for my study because different studies use different types of questions to determine the beliefs, thus, it would have been difficult to design appropriate tests and to compare their results across studies. Also, factors other than health beliefs also profoundly influence health behavior practices such as cultural factors, socioeconomic status, and previous experiences, which are not considered in the health behavior model (Hochbaum, Rosenstock, & Kegels, 1952).

Another potential theory to have implemented for this study was the social cognitive theory (SCT). According to this approach, human motivation and actions are mostly regulated by forethought, and the theory outlines some crucial factors that describe behavior (Schwarzer & Luszczynska, 2005). SCT is limited in that it focuses solely on the dynamic interplay between person, behavior, and environment. Therefore, it is unclear the extent to which these factors affect the outcome behavior and if one is more influential than another (Schwarzer & Luszczynska, 2005). Although the theory was helpful to understand the outcomes and causes of the diseases and other health conditions, it may not be possible for agencies to develop fruitful, targeted CLP prevention programs in the United States.

Limitations

Any study will have some limitations that may be considered weaknesses. The participants selected from the Natality birth certificate data may not represent the entire population of women who delivered live births during that period because some mothers who birthed their children at home were not included in the data base, and women who gave birth to infants outside the United States were also not included in the study. Secondly, researchers may be concerned about the tools used to collect data; the creation of these tools and methods may contain inherent bias and therefore influence study outcomes. Accuracy of the birth data was also considered a limitation for the study. There was also a potential for bias in the birth data due to recall. Since the data was collected after the birth of the baby; it may have been difficult for the mothers to remember whether they had used tobacco or any drugs during pregnancy. If the collected data were not accurate then the information gathered would be of little use or would not be effective in reducing rates of CLP among children in the United States.

However, since I used secondary data from the birth certificate documents, it was impossible to address the limitation of the study. The birth data were self-reported by the mothers, therefore, I could not verify if the women truthfully provided all information when completing the forms, especially concerning variables such as smoking during pregnancy and other medical history. No measure could have been taken to identify whether the information provided was accurate.

Another limitation was the presence of high levels of missing data. The vital statistics data was instrumental for health care professionals in a wide variety of situations such as the administrative analysis and for scientific purposes. Depending on the specific purpose for which the data is used, there can be limitations to this data. Factors limiting the use of data arose from imperfections such as missing data or misclassified data in the actual database or from the impracticability of these data.

A limitation of the data that I noted concerns the completeness of birth registration. It is estimated that 99% of the data were recorded in birth certificates. Another issue was the completeness of reporting. Birth certificate interpretation must include the integrity of the item. I measure the quality of the information in terms of the "not stated" percentage, and the reporting varied among the items reported among different states.

There was also a significant amount of missing data in the Natality data file. The data that were missing and inaccurate were also included in the Natality data file. The high percentage of "not stated" should be used with caution. The data quality issues for the states' specific data were also a concern for the researchers due to inaccuracy or underreporting, and thus should be used with caution. Another limitation was that item wording across states and all the variables were not consistent with the national standard, so I could not consider and compare data for each state with those of other states.

Significance of the Study

This research could fill a gap in identifying several significant maternal risk factors that are predictive of CL with or without a CP. This project was unique because it addressed some of the factors that are linked to both of these orofacial defects since they are both developmental in origin and related to the absence of fusion of nasal bones. This research could also aid in filling a gap in scholarly understanding of the problem by presenting findings specifically related to the etiological relationship of the various factors contributing to this developmental problem. This study of the etiological factors associated with CLP is unique because it shows some of the factors that are predictive and some factors that are under-researched in the area of the developmental problems. The study results could provide much-needed insight into the relationship between risk factors; measures need to be taken to rectify these issues prenatally because children with this defect require significant medical care and incur significant costs (Alkire, Hughes, Nash, Vincent, & Meara, 2011). With the increase in population, the overall infant morbidity and mortality has decreased over the years. A recent research study was needed to determine some of the predisposing factors that are contributing to the outcome of these birth defects among women in the United States. Consequently, this research could lead to social change among women by enabling them to understand and avoid certain prenatal behaviors and engage in early and improved care during pregnancy to develop a healthy baby. Results from this research could help healthcare professionals identify risk factors at an earlier stage during prenatal care so further adverse effects could be prevented. In result, this would help healthcare professionals reduce the cost of treatment for the children who are affected with CL or CP (Alkire et al., 2011). Furthermore, CLP has an extensive effect on the economic well-being of families; those affected may not have sufficient or any insurance to pay for their treatment, thus preventing those with CLP from accessing the best care (Alkire et al., 2011).

Summary

Although research conducted on CLP in the past year indicates that there are prevention methods to minimize its occurrence, rates of CLP in the U.S. have remained high for nearly a decade. Its persistence is indicative of lowered quality of health and well-being within that affected population. Orofacial deformities are a prominent issue for children not only in the United States, but also across the world. Although some research has been done in the past years on the etiological factors of CLP across the nation, no recent studies have indicated the current state of the factors leading to the problem in the United States. Also, there is no ample evidence for other specific risk factors such as reproductive history and use of assisted reproduction during pregnancy, these may be a causative factor for CLP among women. Therefore, in this quantitative study using the epidemiological triad theory, I explored the most predictive etiological factors that are linked to CLP among U.S. resident women who had a live birth in hospitals and birthing centers between January 2016 and December 2016. The specific purpose of the research was to identify the association between maternal behaviors, reproductive history, socio economic status, and rate of admission to NICU.

From the literature review, I concluded that the problem is mainly associated with maternal behaviors during their prenatal period. Therefore, I used epidemiological triad as the primary theoretical foundation for the study. I used this theoretical framework when developing the research questions and hypothesis and deciding on methodology. This framework also provided enough guidance as I interpreted results and identified prevention strategies and areas that need future research. The study’s findings will enable researchers to understand the significance of the problem amongst women across the United States. These findings will enable the healthcare professionals to develop specific prevention programs targeting women and families who are at high risk for developing CLP. The study findings will also help clinicians in developing prevention strategies during prenatal care.

Finally, these findings will help thousands of children and their families suffering from CLP to have an improved quality of life. The objective of this study was to identify the primary etiological factors according to past literature, and to determine risk factors and understand the problems associated with them. To develop this understanding, a thorough review of literature on the topic of CLP was required. Chapter 2 provides a comprehensive literature review on the problem and the factors that contribute CLP among infants.

Chapter 2: Literature Review

Introduction

Non-syndromic CL and/or CP is a common congenital anomaly that produces many adverse effects in the lives of the affected individuals and their families. CLP results in a variety of medical, financial, and psychosocial challenges. Although researchers have identified several risk factors associated with CLP, the literature is inconsistent in terms of identifying the relationship between maternal risk factors and CLP. Such inconsistencies make it difficult to determine whether the incidence rate of CLP is increasing or decreasing in the U.S. population. This uncertainty can adversely affect the prevention and the occurrence of CLP in the United States.

The most pervasive maternal risk factors for developing this congenital anomaly are education, age, race/ethnicity, marital status, tobacco use, alcohol use, and inadequate prenatal care. The purpose of this quantitative, descriptive, non-experimental study was to determine if there is a relationship between CLP and maternal characteristics such maternal reproductive history (advanced maternal age, maternal obesity, number of prenatal visits, month prenatal care began, number of pregnancies, gestational age at birth, assisted reproductive technology used, gestational diabetes, and gestational hypertension), socioeconomic status of the mother (marital status, education, mother's race, payment source for delivery, and place where birth occurred), and admission to the NICU in U.S. hospitals from January 2016 through December 2016. While past researchers have previously examined maternal risk factors for CLP, there is a lack of recent, significant research with no scholarly consensus regarding the impact of maternal demographics, illness, reproductive history, and weight gain on the risk of oral clefts in infants. This study may enable healthcare professionals to identify risk factors at an early stage, implement strategies to reduce these risk factors, and ultimately result in a reduction in CLP rates among infants. Chapter two includes an overview of the literature search followed by a discussion of the theoretical constructs of epidemiological theory, and a discussion of the variables and concepts for this research.

Literature Search Strategy

I performed a systematic literature review of existing research on the relationship between CLP and maternal risk factors such as education, age, race/ethnicity, marital status, tobacco use, alcohol use, and adequate prenatal care. The strategy I used for the literature review involved using multiple databases that I accessed via Walden University Library. These databases included CINAHL, MEDLINE, Google Scholar, PubMed, EBSCO, Medline, and ProQuest Dissertations. The key terms used included *cleft lip*, *cleft palate*, *infant mortality*, and *admission to the neonatal intensive care unit*. Search terms specifically related to the maternal risk factors included *maternal risk factors*, *maternal demographics*, *maternal socioeconomic status*, *maternal infection*, *maternal illness*, *maternal ethnicity and race*, *maternal cleft lip*, *maternal cleft palate*, *maternal characteristics*, *maternal risks*, *prenatal care*, and *pregnancy outcome*. These searches yielded many articles on CLP, however only a few of these articles provided information on the specific focus of my research. Therefore, I used additional resources such as academic and peer-reviewed articles in periodicals, qualified websites, and books.

My goal in the literature search was to obtain articles published within the last 10 years. However, some articles from earlier years offered valuable information as well. I obtained approximately 982 articles published between the years 2000 to 2017. I then conducted an advanced search refined to specific features, which resulted in 20-30 articles for the overall risk factors that are specific to the topic. The search was done primarily due to the dearth in current literature on maternal risk factors and congenital disabilities. When I searched for each of the risk factors associated with CLP, I retrieved only 5-10 articles on each, and some articles were not specific to the variables in my study. My search was limited to those articles published in English.

I also retrieved two dissertations from the Walden University Library database. I conducted a similar search for all dissertations (outside of Walden) using *maternal risk factors*, *cleft lip and palate*, *antenatal care*, and *NICU admissions* as search terms. Since only 20 dissertations were retrieved with those conditions, I searched the reference lists of these dissertations for additional articles. The final articles were selected for literature review only if they addressed maternal risk factors and CLP. I also examined several websites and used the Walden University Library to explore the outcomes of CLP and their relationship to neonatal intensive care admissions.

Theoretical Foundation

Theory provides a basic framework and foundation for the initiation of any research project. Theory also provides the groundwork a researcher needs to identify the methods and directions for a research study (McEachan, Lawton, Jackson, Conner, & Lunt, 2008). Theory also enables the researcher to evaluate how behaviors may be changed and to assess the reasons for the manifestation of these changes. Theory also enables the researcher to recognize whether these changes in behavior are due to the modification of one theory or other. The selection of theory determines and shapes the way a study is constructed.

I used the epidemiological triad theory as the framework to guide this research on maternal risk factors associated with CLP. My study of these risk factors facilitated identification of the relationships and degrees of intensity associated with these risk factors and adverse pregnancy outcomes. Orofacial clefs (OFC) and its associations can be identified through the implementation of the epidemiological theory. However, there is a lack of recent, significant studies on OFC's, and investigators have not reached a consensus regarding the impact of maternal demographics, illness, reproductive history, maternal smoking, weight gain, and the risk of oral clefts.

The epidemiological triad or triangle consists of an external agent, a host, and an environment in which host and agent are brought together, causing the disease to occur in the host. As the CDC (2012) has noted,

> In the traditional epidemiologic triad model, transmission occurs when the agent leaves its reservoir or host through a portal of exit and is conveyed by a mode of transmission to enter through an appropriate portal of entry to infect a susceptible host. Transmission may be direct (direct contact host-to-host or droplet spread from one host to another) or indirect (the transfer of an infectious agent from a reservoir to a susceptible host by suspended air particles, inanimate objects [vehicles or fomites]), or animate intermediaries (vectors). (p. 1)

The concept of the epidemiological disease triad or disease triangle was first formalized in the 1960s by George McNew, a scientist at the Boyce Thompson Institute for Plant Research. According to McNew (1960), the disease triangle could be used to study the relationship between various epidemic factors in a disease and to understand how epidemics might be predicted, limited, or controlled (Scholthof, 2007). The epidemiological triad evolved as researchers used it to identify, understand, reduce, and control infectious diseases in specific populations.

Researchers have used the epidemiological triad theory successfully over the years to study various infectious disease epidemics (Scholthof, 2007). However, during the 1960s and 1970s, there were outbreaks of various non-communicable diseases. Many of the studies on these diseases were behavior-based and targeted such behaviors as tobacco use, drug abuse, injuries, and other ailments. The epidemiological triad was implemented in a minimal number of these studies because of the difficulties in viewing these problems as “true” epidemics and because of the difficulty of defining “vectors” in non-biologically induced diseases (Egger, Swinburn, & Rossner, 2003). In 1980, a paradigm shift occurred when William Haddon effectively used the triad approach to injury prevention. Haddon (1980) recognized the importance of the host, vector, and environment in the “epidemic” of motor vehicle injuries. The use of the epidemiological method paved the way for large-scale reduction in motor vehicle injuries in western countries in the succeeding years (Haddon, 1980). Researchers have also used the epidemiological triangle to address epidemics such as smoking and coronary heart disease, which have declined because of integrated epidemiological approaches.

Swinburn and Egger (2002) stated that the epidemiological triad was an excellent method for studying many non-infectious diseases such as obesity. Specifically, the triad has been useful in identifying the frequency, source, distribution, and patterns of these health conditions in populations (Swinburn & Egger, 2002). Similarly, Egger, Swinburn, and Rossner (2003) used the theory to tackle obesity by ascertaining potential interventional approaches at each level. Researchers have since used the theory of epidemiological triad not only to identify and mitigate the infectious diseases, but also to identify the relationship between specific chronic diseases, such as obesity, and their causes (Flegal, 2010).

The epidemiological triad theory was a good fit for identifying the association between maternal risk factors and CLP. I could use the same analogy other researchers used when identifying chronic diseases to identify the risk factors that are predictive of CLP in the U.S. population. This study on maternal risk factors was an epidemiological retrospective, non-randomized study. Using the epidemiological triad theory, I built the study on the premise that a mother's behavior and actions can contribute to congenital anomalies in the newborn. The covariates used for the study comprised the three aspects of the epidemiological triad: agent, mode of transmission, and the host.

In the epidemiological triad model, the agent is the causative factor for the disease (Dicker, 2008). The agents or the etiological factors in this study are maternal smoking, maternal education, prenatal care, income, maternal illness and reproductive history, and maternal race/ethnicity. The reservoir is what houses the agent (Dicker, 2008). For this study, the reservoir is the mother, and the host is the infant. The mode of transmission is defined as the transfer of the agent to its host using a direct, indirect, or vector-borne method (Dicker, 2008). In this circumstance, the mode of transmission is the placenta through which the causative agents are passed to the infant. This type of transfer to the infant can be either through direct method (maternal obesity or maternal tobacco use) or through indirect means such as maternal demographics, income, age, education, maternal prenatal care, or a vector-borne method (ill mother). I considered the infant as the host since the cause of CLP in the infant is also due to advanced maternal age, maternal illness, maternal behaviors, and decisions made by the mother. Therefore, I worked to understand these risk factors and researchers' use of the epidemiological triad theory for successfully controlling and reducing these risk factors in other chronic diseases.

Literature Review Related to Key Variables

This chapter provides information about some of the research that was conducted previously on CLP that are both modifiable as well as un-modifiable. The maternal risk factors I studied include advanced maternal age, race/ethnicity, income and education, smoking, prenatal care and reproductive history, maternal infectious diseases and maternal behaviors.

Women could avoid adverse birth outcomes if they take care of their health prior to conception and during pregnancy. Preventing specific behaviors is also key to having a healthy baby. In this study, I explored the influence of maternal characteristics, maternal behaviors on CLP among women in United States. This topic is important because an improved understanding of the causative factors will enable medical professional to identify and manage these problems at an earlier stage, to avoid developing these congenital anomalies in some infants. The literature review on maternal risk factors aided in determining the maternal risk factors that are most predictive of CLP from the studies conducted previously. The data for the study was extrapolated from the available CDC vital statistics data between January 2016 and December 2016.

Maternal Risk Factors Linked to Cleft Lip and Cleft Palate

Numerous maternal risk factors are linked to congenital anomalies such as CLP in infants. The most significant and common risk factors include demographic factors such as advanced maternal age, maternal race /ethnicity, maternal education, and income (Angulo-Castro et al., 2017). Biological factors include gestational diabetes, gestational hypertension, pre-pregnancy diabetes, pre-pregnancy hypertension and eclampsia, infections such as gonorrhea, syphilis, chlamydia, chorioamnionitis, antibiotic and steroid use during pregnancy, and reported maternal morbidity (Nagalo et al., 2017). Risk factors are also present in maternal behaviors such as maternal tobacco use in the first, second and third trimesters of pregnancy, obesity, and weight gain during pregnancy (Wehby et al., 2017). Maternal reproductive history such as some prenatal health care visits, the timing of pregnancy care, the number of previous pregnancies, gestational age at birth, the number of previous live births, and previous preterm deliveries, previous pregnancies resulting in infant congenital anomalies, a history of infertility treatment used, use of fertility enhancing drugs, and assisted reproductive technology (Shibui et al., 2016).

An additional risk factor is the mother's socioeconomic status (SES) and the impact it has on the rates of ACLP, which may lead to an increase in healthcare costs due to admissions to the NICU. Higher rates of cleft lip and palate indicate that these issues are public health in nature due to lack of adequate maternal nourishment, health-diminishing conditions and lack of proper health and wellbeing (WHO, 2010).

An extensive literature review revealed that the cause of CLP is comprehensive and interconnected components such as social factors, genetic predispositions and environmental exposures are included (Charugundala, 2013). Charugundala also identified social factors, which include, but are not limited to, racial/ethnic variation, maternal age and socioeconomic status (SES). Furthermore, high maternal age and low SES are factors associated with elevated risk of clefting (Charugundala, 2013). Genetic predisposition includes maternal and fetal genes and gene products that may be responsible for increased risk of CLP (Watanabe et al., 2006). However, to prevent CLP among population that has a genetic predisposition, it is impossible to have the gene modification, but the effect of gene can be minimized with genetic counseling, intake of vitamin supplements and prevention of risk factors (Watanabe et al., 2006). Finally, environmental exposures include, but are not limited to, cigarette smoking, alcohol consumption, maternal stress, prescription drugs (Charugundala, 2013). However, all these risk factors are either modifiable through personal choice or prevention strategies or can be reduced with pregnancy planning, as is the case with social factors and genetic predispositions. Lifestyle modification as well as a focus on the advanced research in these areas will be the most efficient way of preventing clefts (Mossey, Davies, & Little, 2007). Lifestyle factors, which include pregnancy planning, proper nutrition and avoidance of preventable and modifiable risks that include excessive tobacco use and consumption of alcohol are imperative in minimizing the prevalence of clefts (Mossey et al., 2007). The researchers also imply that prevention efforts have been fragmented. Therefore, this thesis provides an extensive literature survey to identify a new direction of research (Charugundala, 2013).

Maternal Socio-Demographic Status

Maternal socio-demographics such as age, race /ethnicity, education, migration history, education, and income may have some indirect consequence for the development of CLP (Angulo-Castro et al., 2017). Previous research studies indicate that societal status is a dependable predictor of the anomaly and infant mortality (Kawachi, 2000). Moreover, it has been established that there is a relationship between social status and health status. A higher economic condition is usually associated with improved health and wellness (Kawachi, 2000: Lynch & Kaplan, 2000). This is indicated by the “social gradient in health” which states that social status inequalities are indicative of dissimilarities in the health status of the people that are not related to dissimilarities in societal status (Morales-Suárez et al., 2009). The exact mechanism regarding the association between the discrepancies in SES is unknown. However, the first step toward addressing the issues is to assume that socioeconomic factors include a wide array of public and monetary conditions (Morales-Suárez et al., 2009). Acuña-González et al. (2011) indicate there is a meaningful relationship between SES and locality of birth. The results of the survey indicate that CLP increases as the as socioeconomic position decreases (Acuña-González et al., 2011). However, since the mechanism or indicators of each of the etiological agents may be dissimilar for every individual, additional inquiries are necessary to enhance the knowledge and understanding and to determine if these congenital anomalies center around certain maternal behaviors such as maternal smoking, maternal obesity, maternal illness, or prenatal care (Acuña-González et al., 2011). A prevention study using data from National Congenital Disabilities Registry from 1997-2000 also revealed that the SES of the individual or family plays a significant role in congenital anomalies such as OFCs, neural tube defects, and congenital heart defects (Yang, Carmichael, Canfield, & Song, 2007). The researchers evaluated both maternal and paternal income, education, and occupation to measure SES. The researchers found that elevated risk of the birth defect was consistently observed in individuals with the lowest household income (Yang et al., 2007).

Distribution of demographic characteristics is identified in infants with birth anomalies. Low SES includes a broad range of factors such as nutritional status, several socioeconomic and socio-demographic factors. The authors, Angulo-Castro et al. (2007) recommend a pro-active counseling and prevention program for families at risk for non-syndromic CLP. The researchers indicated the likelihood of CLP cases are more likely to have low SES and most of the cases live in rural areas where birth took place at home or in a hospital administered with public funds as opposed to privately owned hospitals, or they did not have adequate insurance coverage or treatment choices (Angulo-Castro et al., 2017).

Socioeconomic measures that collectively include income, occupation, employment, educational status and poverty are factors that may be linked to CLP (Carmichael, Nelson, Shaw, Wasserman, & Croen, 2003). Research findings also indicate that there are other factors such as lack of consumption of multivitamin, use of tobacco and consumption of alcohol are other risk factors of CLP (Carmichael et al., 2003). However, this study found that low SES was not directly linked with the risk of orofacial palate (Carmichael et al., 2003). Swedish researchers who conducted a study between 1976-1977 using birth registry data concluded that the risk and susceptibility of clefting is higher among a population with low SES (Ericson, Eriksson, & Zetterstrom, 1984). Conversely, researchers in Scotland indicated that there is a relationship between OFC's and SES; however, the researchers failed to account for confounding factors such as tobacco use and certain other preventable risks (Womersley & Stone, 1987). Furthermore, it is interesting to note that low SES is not a significant risk factor of clefts when the researchers were able to account for these confounders (Womersley & Stone, 1987). When adjusting for other various risk factors, it is evident that low SES does not significantly increase the risk of clefts, however, there are associated risk factors with SES that cause an increased risk. Preventable behaviors such as smoking and alcohol consumption are more common among people with low SES and thus must be the focus of educational interventions and nutritional supplementation (Van Oers, Bongers, Van de Goor, & Garretsen, 1999). According to Mossey, Davies, and Little (2007) people with low SES are less educated, therefore the key to overcoming risk factors is increasing pregnancy planning and eliminating toxic environmental substances. Low SES is typically a result of low economic standing but is not necessarily an indicator of maternal education levels.

Research in Hungary revealed there is the higher rate of OFC amongst infants of unskilled workers and homemakers as compared to professionals **(**Puho, Métneki, & Czeizel, 2005). In addition, the same study indicates that maternal education is not a factor in SES standing. However, it is impressive to note that parental schooling and a high rate of OFC are highly interrelated (Charugundala, 2013). Nonetheless, it is evident that educational disparities are the reason for accidental pregnancies, but a causal relationship has not been established (Finer & Zolna, 2011). Since the exact relationship between SES and CLP is not known and it is hard to determine the cause of CLP, researchers should continue to discover the likelihood that SES can be a risk factor. The results were not constant, but we do know that preventable factors such as alcohol consumption and smoking can be more prevalent in populations with low SES. Thus, Puho, Métneki, and Czeizel (2005) concluded that these socioeconomic factors such as income, schooling, employment, occupation, and poverty are not directly associated with increasing OFC, but they add to the uncertainty in addition to other factors.

Family planning is much lower in individuals with low SES, which increases the risk of adverse health outcomes, however, whether these outcomes such as CLP results from inadequate nutrition or increased exposure to teratogens is unclear (Dehlendorf, Rodriguez, Levy, Borrero, & Steinauer, 2010). Several studies indicate that there are a few other factors that must be considered while analyzing these studies. Many of these studies were conducted in a variety of countries and geographic regions, which exposed differences in health care, pregnancy planning, pregnancy education, and exposure to potential teratogens (Charugundala, 2013). The study methods also varied for many studies including control classification and selection as well as limited sample size in some studies. Therefore, while the exact relationship between SES and risk of clefts has not been determined, researchers should continue to explore the possibility that SES can be a risk factor.

Advanced Maternal Age

Advanced maternal age, race, level of education, and income have a significant impact on congenital anomalies including as well as CLP. Researchers found that paternal age is a contributing factor to many birth defects occurring in their children (Auroux et al., 2009). These researchers also found that advanced maternal age can lead to low progeny height and mental aptitude (Auroux et al., 2009). The researchers also found a correlation between maternal age above 30 and increased risk of delivering infants with Down syndrome (Erickson, 1978; James et al., 1999). Contrastingly, younger maternal age was also associated with gastroschisis and premature births (James, et al., 1999). Maternal age was found to have a significant effect on the development of congenital anomalies. Therefore, researchers should be exceptionally vigilant to explore the association between age and CLP (Charuguntala, 2013).

Advanced maternal age influences the adverse birth outcome in infants, thus the older the mother the greater chance the infant has to be born with congenital anomalies (Myrskylä & Fenelon, 2012). This can be interpreted as the physiological process that is related to the superior maternal agent that decreases the quality of the oocyte. In a recent study conducted in the United States with a large sample size of the American female population, researchers revealed that infants born to mothers below 25 and over 35 years of age have negative outcomes regarding their health, height, weight and risk of obesity (Myrskylä & Fenelon, 2012). Some adverse health conditions have also been diagnosed in those mothers who have infants when they are below 24 and above 34 years of age. Therefore, the researchers concluded there is a definite link to the age of the mother and adverse offspring outcome (Myrskylä & Fenelon, 2012). Several other researchers also found that advanced maternal age is a risk factor for OFC (Shaw, Croen, & Curry, 1991). The researchers found that women who were 39 years of age or older were twice as likely to have children born with clefts than women between 25-29 years of age (Shaw, Croen, & Curry, 1991). Conversely, it is interesting to note that some researchers whose studies had larger sample sizes and effective measures to control those confounding elements, such as tobacco use and alcohol intake, could not discover a significant connection between higher maternal age and oral cleft malformations (Abramowicz, Cooper, Bardi, Weyant, & Marazita, 2003; Vallino-Napoli, Riley, & Halliday, 2004). A meta-analysis conducted on eight population-centered research studies show that increased maternal age is not related to oral clefts (Vieira, Orioli, & Murray, 2002).

It is also interesting to note that younger mothers (14-19 years of age) had a significantly higher risk of delivering infants with clefts and that women who wait to give birth until they are in their 20's reduce the risk of delivering infants with clefts (Reefhuis & Honein, 2004). According to some recent studies, a lowered SES can lead to limited access to prenatal care including limited access to prenatal vitamin supplements as well as other planning measures which place younger mothers at a greater risk of delivering infants with clefts. These mothers may not be able to adequately prepare for their pregnancy and may be unable to consume nutritious food in preparation for the birth of their babies. However, these recent studies failed to efficiently account for confounding factors, therefore, the researchers concluded that there may be associated risk factors such as SES that are more likely to be responsible for the increased risk (Reefhuis & Honein, 2004). Alternatively, on a molecular level, DNA hypomethylation and nutritional deficiencies are associated with both very young mothers and mothers above the age of 35, which explains the relationship between maternal age and clefts (Charugundala, 2013). In older mothers, DNA hypomethylation can be a result of decreased genome integrity and reduced capacity of DNA methyltransferases. Hypomethylation can occur in very young mothers as they are still growing, and their own needs can compete with the fetus or nutrients (Charugundala, 2013).

Research indicated that advanced maternal age is a factor related to lifespan and overlaps shared weakness or investment of the parents and sometimes it is not directly linked to the maternal biological well-being at the time of conception, growth, and development of the fetus or delivery (Myrskylä & Fenelon, 2012). These researchers also suggested that it is not ideal to deliver at a very young age, rather it is preferable that the adolescent mother wait for a few years to increase the chances of delivering a healthy baby (Myrskylä & Fenelon, 2012).

Maternal Race

Maternal race is another factor that determines CLP development among infants in the United States (Vanderas, 1987). Researchers studies impacts on maternal and paternal effects on the incidence of oral clefts among the Caucasian and African

American populations in the United States and indicated that the prevalence and the rate of oral clefts were higher in children of Caucasian mothers as compared to African American mothers after father's race is adjusted. (Thériault, Iturra, & Gingras, 1983). The researchers concluded that the difference in the reported number of cases of CLP between Caucasians and African Americans is due to the influence of maternal race. However, it was difficult to attribute the independent effect of mother or father's race on the difference in the regular rates of CP (Thériault et al., 1983).

Researchers suggested that racial and ethnic differences have a direct link to many health-related issues and congenital anomalies in infants, some of which are spina bifida, CLP, increased cancer risk and muscular malformations (Boulet, Gambrell, Shin, Mahonein, & Mathews, 2009). Racial disparities can be attributed to confounding factors and may not have any association with OFC when reviewed independently (Berger, Zhu, & Copeland, 2003). Therefore, additional studies have been done to identify the association between scientific evidence, and racial or ethnic differences to determine if there are any associations with OFC.

Researchers conducting an epidemiological study in Mississippi concluded that the risk of CLP is higher in the Asian population with 14:10,000 births, the Caucasian population with 10: 10,000 births, and African Americans have a chance of 4:10,000 births (Das, Runnels, Smith, & Cohly, 1995). Researchers who conducted a study in California found that black, non-Hispanic infants had a lowered risk for OFC as opposed to white, non-Hispanics (Shaw, Croen, & Curry, 1991). Contrariwise, studies that were conducted in Washington and Pittsburgh, researchers demonstrated that there is more susceptibility for African-American mothers to have children born with clefts as compared to Caucasian mothers (DeRoo, Gaudino, & Edmonds, 2003). Also, the Hispanic population in Texas was found to have a higher incidence of CL (Brender, Suarez, & Langlois, 2008). Finally, a study conducted in Australia shows that the Australian aboriginal population is at higher risk of clefting than the Caucasian Australian population (Bell et al., 2013). Most of these studies on maternal race were limited geographically and, due to accessibility of the data, were limited to specific regions. Therefore, it is likely that while it is most practical to conduct population studies with a limited geographic scope, this, along with confounding factors, most likely accounts for the racial/ethnic differences when examining potential maternal risk factors of CLP. Data limitations and relatively disproportionate comparability create challenges when assessing the genetic risk in the study population. Due to the conflicting results obtained when the researchers conducted studies on racial and ethnicity, the researchers concluded that no ethnic group is more susceptible to have infants with oral clefts (DeRoo et al., 2003). There were conflicting results when the CLP were linked to race and ethnicity. Moreover, these researchers only examined the specific population and failed to assess additional factors. For example, the differences between African-Americans and Caucasians produced contradictory results. Possible lifestyle factors such as maternal tobacco use, proper vitamin supplements, and healthy diet were not assessed by the researchers in the study. However, in the context of race, social influences are more likely to play a role than genetic predispositions (DeRoo et al., 2003). Therefore, while it may be useful to know which populations are more susceptible to OFCs, far-reaching and convincing racial and ethnic differences do not exist. For instance, in some areas, the African-American community has less access to health care than Caucasian people, which may result in less than desirable lifestyle factors. Because the social factors are primarily important, increasing pregnancy planning and counseling efforts in high-risk populations may be an effective means of mitigating cleft risk (Charugundala, 2013).

Maternal Biological Factors Linked to Cleft Lip and Cleft Palate

Maternal biological facets which are interrelated to OFCs include gestational diabetes, gestational hypertension, pre-pregnancy diabetes, pre-pregnancy hypertension, eclampsia, previous cesarean section, infections such as gonorrhea, syphilis, chlamydia, chorioamnionitis, and antibiotic and steroid use and reported maternal morbidity (Nagalo, Ouédraogo, Laberge, Caouette-Laberge, & Turgeon, 2017). OFCs are defined as congenital anomalies featuring interruption of a standard structure and abnormal facial growth during the initial gestational period between six to eight weeks, forming a cleft in the lip or the palate. It is one of the most common birth anomalies that comprises a structural weakness and is considered as a significant public health issue. Although there are inconsistencies in the results on the maternal biological factors that are linked to CLP in some studies, other researchers identified a strong association between risk factors such as diabetes, preexisting diabetes mellitus (DM), hypertension, maternal obesity and underlying metabolic abnormalities with CLP. Researchers also concluded that hypertension may also have an impact on congenital anomalies, however the literature on these risk factors associated with OFCs is limited (Kutbi, 2014). A comparative study was conducted on mothers who had infants with OFCs as compared to those without

OFCs to identify the connection between diabetes or gestational diabetes, hypertension, maternal obesity (Kutbi, 2014). The researchers discovered that there is a strong association between maternal obesity and increased risk of OFCs. The researchers also found that mothers who are obese as well as mothers who are underweight have a higher risk of delivering an infant with OFC (Maneerattanasuporn 2017; Kutbi, 2014). More of this type of OFCs are associated with a decreased maternal education level. Also, compared to the healthy mothers, the risk of OFCs increases when there was a combination of maternal obesity or underweight (Cedergren & Källén, 2005). The researchers indicated that since there is a connection between diabetes, obesity, hypertension, and the increased incidence of OFCs, expectant mothers are encouraged to follow healthy habits, nutritious diet, maintain a healthy weight, and take measures to be screened for probability of diabetes or hypertension before outset and during initial stages of pregnancy (Kutbi, 2014).

In a recent study, researchers concluded stressful situations in the families of pregnant women as well as contracting infectious or non-communicable diseases during the first trimester of pregnancy, and the use of medications during this period, have some impact on the development of these malformations (Chincharadze et al., 2017). Metneki, Puho, and Czeizel (2005) suggested that the presence of maternal infections during pregnancy increases the risk of delivering an infant born with CLP (Metneki, Puho & Czeizel, 2005). The researchers also recommended that additional studies are required to establish an underlying biological mechanism associated with CLP (Acuña-González et al., 2011). Researchers who conducted a survey in West Africa to assess etiologies linked to congenital anomalies as well as related medical disorders in children with OFCs, indicated that maternal medical conditions such as anemia, infections, malnutrition, and hemoglobinopathies have an impact on CLP. It is common to have medical co-morbidities and congenital anomalies in infants with OFCs. The researchers concluded that further investigation is required and recommended to have a National Malformations Registry to improve the understanding of OFCs (Nagalo et al., 2017).

A study conducted in Pakistan conducted by Hamid, Khattak, and Ambreen (2017), indicated the relative incidence and types of congenital anomalies in the offspring of women suffering from medical problems during pregnancy. A sample of 1,000 women admitted for delivery was included in the study and particularly the cases of congenital anomalies were studied. The results of the survey indicated that there were medical problems in mothers who had infants with CL with 20.28% of the mothers suffering from hyperpyrexia due to various bacterial and viral infections (Hamid, Khattak, & Ambreen, 2017). Other conditions include TORCH infections, hypertension, diabetes mellitus and cardiovascular problems, psychosocial problems, and epilepsy (Hamid et al., 2017). The congenital anomalies in infants in the population studied included CL/CLP, clubfeet, and ventricular septal defect, meningocele, hydrocele, polydactyly, undescended testis, congenital cataract and intracranial calcification. Several risk factors can be avoided if necessary precautions are taken on time (Hamid et al., 2017). Therefore, during pregnancy, women with illnesses such as diabetes, cardiac diseases, hypertension, epilepsy, hyperpyrexia, and various psychosocial problems should be timely and adequately treated with safe drugs, having no teratogenic effects on the fetus (Hamid et al., 2017).

Thottumkal and Deepak (2013) conducted a study in India to identify the overall incidence of congenital anomalies to enhance the public awareness of infants born with congenital anomalies. The study emerged due to the need to determine a mechanism for the prevention of physical and mental disabilities and the even the fatal outcome encountered by the families. Therefore, the cause was initially identified. Researchers indicated that the infants born with CLP are highest in India. The researchers also found that the most common congenital anomalies observed in India included CL, CLP, autism, muscular dystrophy, Down syndrome, neural tube defects and congenital heart disorders (Hamid et al., 2017). The significant etiological factors for developing birth defects include consanguineous marriage, low birth weight, advanced maternal age, and low SES (Hamid et al., 2017). Maternal infections such as syphilis and rubella as well as multiple births were also significant factors contributing to the development of congenital anomalies in India. Counselling sessions are not available in many areas of the country (Hamid et al., 2017). The researchers indicated that mothers who participated in counseling sessions may have a substantial improvement in pregnancy outcome and recommended that pregnant women participate in prenatal counseling (Thottumkal & Deepak, 2013).

Maternal Personal Behaviors and Cleft Lip and Palate

Maternal behaviors such as tobacco use have a significant effect on CL and CP. Tobacco products contain a potent teratogen called nicotine which forms causative factors which result in transformations and growth delays in a fetus t the developmental stage (Ozturk et al., 2016). In an experimental study in mice, researchers proved that continuous nicotine administration caused retardation in development, low birth weight, stillbirths and noteworthy abnormalities in the shape and size of the palate, as well as a persistent midline epithelial seam in the pups (Ozturk et al., 2016). Furthermore, nicotine exposure was found to affect approximately 46% of the CP-causing genes. The researchers concluded exposure to nicotine during pregnancy hindered the healthy growth and development of the fetus. It also resulted in the formation of a persistent midline epithelial seam with type B and C patterns of palatal fusion (Ozturk et al., 2016).

A recent study was conducted in Mexico to identify the maternal risk behaviors that are linked to the development of CLP (Pons-Bonals et al., 2017). The researchers found that demographics and maternal behaviors such as, poor nutritional intake, smoking, misuse of alcohol, recreational drug usage and a history of sexually transmitted infections are some of the causes of maternal behaviors linked to the development of CLP (Pons-Bonals et al., 2017). The researchers analyzed multiple variables such as birth weight, gestational age, tobacco use, alcohol use, folic acid and multivitamins use during pregnancy, recreational drug use, sexually transmitted infections, marital status, and SES (Pons-Bonals et al., 2017). However, the researchers concluded that some of these factors were related to the formation of CLP (Angulo-Castro et al., 2017). Several researchers concluded some of the similar maternal risk factors associated with the development of the congenital anomaly. Smoking-adjusted by weight significantly raised the risk of orofacial anomalies (Pons-Bonals et al., 2017). The researchers revealed the need to standardize the data registration on medical records to improve the monitoring and treatment of patients and emphasize actions to maintain low incidence of CLP (Pons-Bonals et al., 2017).

Maternal Tobacco Use

Wehby et al. (2017) suggested that maternal smoking and body mass index (BMI) interactions were a contributing factor to the risk of oral clefts. The researchers found a significant negative smoking-BMI interaction, cleft risk with smoking declining with higher BMI. The researchers also indicated that smoking among underweight mothers was associated with oral clefts in infants, although the smoking-BMI interaction is strongest for CLP only and CP alone (Wehby et al., 2017). BMI was not predictive of the effects of smoking; a clinically relevant increase in smoking-related cleft risk was still present among heavier women (Wehby et al.2017). Researchers used an Atlanta-based congenital disabilities case-control study to identify the association between maternal cigarette smoking and the risk of oral clefts in offspring (Khoury, Gomez-Farias, & Mulinare, 1989). Exposure to smoking was defined as reported preconceptional maternal smoking that includes three months before conception versus three months after the beginning of pregnancy (Khoury et al., 1989). The researchers found out that the children of smoking mothers were 1.6 and 2.0 times to have a baby born with the isolated cleft lip with or without cleft palate as compared to nonsmoking mothers. It is also interesting to note that the offspring of smoking mothers were not at higher risk of having a baby born with cleft lip and palate and associated birth anomalies (Khoury et al., 1989).

Another study was conducted in Maryland, between 1992 to 1998, to identify isolated, nonsyndromic oral clefts (Beaty et al., 2001). The researchers used cleft cases as well as unaffected controls to identify the genetic and environmental risks. DNA samples were obtained from all the cases, their parents as well as the controls (Beaty et al., 2001). It is surprising to note that the researchers found no significant difference between risk factors such as vitamin use, maternal smoking, infection, or recreational drug use after adjusting for maternal age and education (Beaty et al., 2001). The use of alcohol during the critical period of pregnancy (i.e., one month before conception through the first trimester) was reported to occur more often in the control group compared to case mothers. The researchers also found a genetic risk factor where there is a 10-fold increase in risk to siblings of cases as compared to siblings of controls (Beaty et al., 2001).

Preconception cigarette smoking has been documented in numerous worldwide studies as the cause of adverse health outcomes (Levy et al., 2013). Cigarette smoking increases the risk of low birth weight, placenta previa, and fetal mortality (CDC, 2004). Fetal craniofacial development is particularly sensitive to the teratogenic effects of maternal cigarette smoking and thus should be monitored closely (Shi et al., 2007). Interestingly, a few studies reported that tobacco use during pregnancy was considered an insignificant risk factor for oral clefting in the offspring (Wyszynski & Wu, 2002). Another researcher supported this assertion by only finding a slight positive dose-response (Lieff et al., 1999). Contrastingly, maternal smoking has been shown to have a statistically significant association with OFC (Honein, 2007). A positive dose-response relationship further suggests the causal relationship between the two (Chung, Kowalski, Kim, & Buchman, 2000). A combination of maternal smoking and variations in maternal/infant genes can increase the risk of developing OFC, more often than those risk factors independently. While it is commonly believed that maternal exposures have the greatest impact on infant health, maternal cigarette smoking has also been implicated with the higher risk of oral clefting due to reduced sperm health (Zhang, Savitz, Schwingl, & Cai, 1992). Smoking and folate deficiencies are associated with higher concentrations of intracellular homocysteine, which is correlated with an increased risk of oral clefting (Shaw et al., 2005). Endothelial nitric oxide synthase (NOS3) regulates homocysteine levels and can be suppressed by cigarette smoking, elucidating another potential mechanism involved in the folate pathway (Shaw et al., 2005). The mechanism remains unclear, but NOS3 likely potentiates homocysteine concentrations by modulating the folate metabolic pathway (Shaw, et al, 2005).

Some researchers have reported that maternal smoking does not independently have a detrimental effect on infant risk of clefting but is a risk factor when propagated by a genetic element (Wyszynski & Wu, 2002). One of these gene variants is N-acetyltransferase1 (NAT1), which when carried by infants whose mothers smoked during the periconceptional period, are associated with a twofold higher risk of developing OFC (Lammer, Shaw, Iovannisci, Van Waes, & Finnell, 2004). Accounting for confounding factors, in one study, Asians and Caucasians were at higher risk of clefting than Hispanics and African Americans, while other studies report the opposite (Brender, Suarez, & Langlois, 2008). There are no conclusive associations between race and clefting. Therefore, it is difficult to associate ethnic differences, NAT1 activity, and clefting. Interestingly, racial differences can account for variation in the metabolism of cigarette toxicants (Haiman, 2006). Independent of smoking, changes in NAT1 activity do not account for racial differences in oral cleft risk (Haiman, 2006).

Transforming growth factor-alpha (TGFA) is a family of growth factors coded by a gene located at chromosome 2p13 and is the first gene suggested to be involved in the occurrence of OFC (Ardinger et al., 1989). TGFA is found at enormous levels in epithelial tissue of the palatal shelves during shelf fusion and is thus potentially important in palate development. Researchers in three studies supported the role TGFA and adjacent DNA regions play in contributing to the occurrence of clefting (Jugessur, 2003). Conversely, no association between TGFA and OFC were found in two studies (Passos-Bueno et al., 2004). In addition to an independent genetic effect of TGFA, there is also evidence that the combination of TGFA mutations and maternal smoking can increase the risk of OFC (Shaw et al., 1996). While maternal smoking exposures influence the presentation of OFC alone, researchers who conducted two other studies reported that there was no association between TGFA genotype and interaction with maternal smoking (Zeiger, Beaty, & Liang, 2005). If the mother reported smoking, there was an overall increased risk of OFC, but that effect was independent of TGFA mutation status (Zeiger et al., 2005).

Maternal Use of Steroids

Use of steroids during pregnancy is another probable causative factor for CLP. The use of topical steroids during pregnancy is indicated, but the safety is still unclear

(Chi, Mayon-White, & Wojnarowska, 2011). A database from the United Kingdom general practice was used to conduct to examine the maternal exposure to topical corticosteroids and its effects on adverse birth outcomes (Chi et al., 2011). The study used data collected from 35,503 expectant women who used prescribed topical corticosteroids between the period from 85 days before last menstrual period (LMP) to delivery or fetal death and 48,630 unexposed women. The researchers found no associations between OFC, CLP/ CP, preterm delivery or fetal death and maternal exposure to topical corticosteroids (Chi et al., 2011). There were similar findings when eliminating exposure before LMP. Conversely, there was an association between fetal growth restriction and maternal exposure to very potent topical steroids shortly before and during pregnancy. The researchers recommended increased development of growth restrictions should be considered and appropriate care provided when very potent topical steroids are prescribed to pregnant women, as well as the provision of proper obstetric care (Chi et al., 2011).

Maternal Reproductive History and the Link to Cleft Lip and Cleft Palate

Maternal reproductive history includes the number of prenatal visits, initiation of prenatal care, number of pregnancies, gestational age at delivery, number of previous live births, previous preterm delivery, earlier babies with congenital anomalies, infertility treatment used, fertility-enhancing drugs used and assisted reproductive technology (Shibui et al., 2016). In the United States births due to assisted reproduction technologies (ART) is >1% and therefore it is essential to identify the association of ART with congenital disabilities (Reefhuis et al., 2008). The study was based on data from the

National Birth Defects Prevention Study from October 1997–December 2003 and the results were compared with mothers who used ART (IVF or ICSI) as compared to those who had unaided conceptions (Reefhuis et al., 2008). The researchers indicated the use of ART was related to septal heart defects, and cleft lip with or without cleft palate among single births. However, there was no significant association between ART and any of the birth anomalies among multiple births. The researchers indicated that some anomalies are found more often in infants who are conceived with ART (Reefhuis et al., 2008). Although the mechanism is not precise, couples considering ART should be informed of all potential risks and benefits (Reefhuis et al., 2009). Researchers showed that advancement in technology has enabled in prenatal diagnosis of CL and CLP and it is imperative to provide the parents with mental health care after diagnosis of CL and CLP based on ultrasonography (Shibui et al., 2016). The researchers also discussed diagnoses, treatment process and prenatal counseling in cases of CLP and the way parents receive prenatal counseling, as well as reassurance to the parents that postnatal support will be provided, right from the start (Shibui et al., 2016). Researchers demonstrated the importance of prenatal diagnosis of CLP as well as the significance of prenatal counseling that is required to provide a positive experience with the delivery of a child with CLP (Dealbated & Hall, 2000). Researchers who conducted a study in Pakistan revealed that consanguineous marriage was found to be a factor and that parental counselling was received in 32 percent of parents with babies with cleft (Elahi et al., 2004). The mothers also received monthly examinations and regular laboratory testing during the entire pregnancy period (Elahi et al., 2004). The researchers found a positive association between increased maternal gravidity and an increased risk of congenital heart defects and isolated cleft lip with or without cleft palate (Elahi et al., 2004). However, the researchers could not support that the maternal history of miscarriages had any effect on the increase in the risk of congenital heart defects, CL or CLP in the infant. The researcher also recommended further studies to provide additional evidence for other isolated congenital anomalies (Materna et al., 2011).

Prenatal Care

Prenatal care is an essential aspect at the time when a woman discovers she is pregnant (Jones, 2002). It is natural for most of the couples to anticipate the birth of a healthy and structurally normal baby, although it is a known fact that 3 to 4% of all pregnancies result in a child born with either a congenital anomaly or a genetic problem (Jones, 2002). The expectation for prenatal care is that pregnant women start care a soon as possible to prevent any potential adverse birth outcomes. Although preconception care is a good practice to follow, regardless of the availability of preconception care, it is always better to start care as early as possible. Prenatal care includes health care services that are received by the expectant mother during pregnancy until childbirth to support and promote maternal health as well as the fetal well-being.

Prenatal care encompasses comprehensive care during pregnancy. Various aspects of prenatal care include a thorough assessment of the mother, risk assessment such as a total medical, surgical and reproductive history, laboratory tests, physical examination, psychosocial evaluation, fetal growth assessment as well as the tests required to confirm it, and assessment of general wellbeing through a step by step examination, procedures, and the process. According to Fowler and Jack (2003), these factors will improve the health-related behavior, services, and social support. Ideally, the initial visit should start during the preconception period, or at least before the first prenatal visit to obtain a baseline assessment of all the investigations and assessments of the mother before the conception (Mills, Rhoads, Simpson, Cunningham, Conley& Las1989). Each prenatal visit should be considered extremely vital, as the requirements of prenatal care are valuable to convey accurate expectations to the parents and their families (Atrash, Johnson, Adams, Cordero, & Howse, 2006; Johnson et al., 2006). Prenatal care also includes the vital procedure to check for certain illnesses through such diagnostic tests as blood glucose, blood pressure, laboratory tests to screen for any sexually transmitted disease and venereal diseases, psychosocial evaluation and evaluation (Atrash et al., 2006; Johnson et al., 2006). Prenatal care also includes treatment of existing medical conditions, other interventions as needed and regular follow up of the expectant mother throughout her pregnancy (NIH, 1989). A study conducted in 2011 in Latin America focused on the importance of prenatal care and compared the role of both private as well as public health sectors in the provision of healthcare services to women (Arrieta, Garcia-Prado, & Guillen, 2011). Six different countries and their services were included in the study and researchers used demographic information and health surveys to assess and compare prenatal care (Arrieta et al., 2011). The factors that determined the place to obtain prenatal care included education, occupation, age, parity, family size, and wealth assessments. The study results from the Latin American countries were broken down into the percentage of prenatal visits. The percentages of prenatal visits in these countries were 20.8% in Guatemala, 17.9% in Bolivia, 14.5% in Nicaragua, 8.3% in Colombia, 6.3% in Peru and 3% in the Dominican Republic (Arrieta et al., 2011). The prenatal visits were classified as underuse or overuse. The researchers indicated that the private sector provides more of the prenatal visits and tests, but that it is not an indication of an improved birth outcome (Arrieta et al., 2011).

Jones (2002) indicated that prenatal diagnosis is a better means of identifying CLP. The diagnosis of CLP prenatally indicates that it is always possible to identify craniofacial abnormalities on ultrasounds performed during the prenatal period. Detection of CLP using ultrasound during pregnancy provides a framework for the clinician to provide counseling to those parents whose infants will be affected (Jones, 2002). Furthermore, ultrasound is always considered an accurate means of obtaining the first picture of the baby and parents may not expect to have any abnormalities in their baby. There are psychosocial problems associated with prenatal diagnosis of CLP that begins initially as a shock accompanied later by anxiety, anger, guilt, and sadness during pregnancy since the couple most likely anticipated a normal infant (Jones, 2002). Therefore, the diagnoses in the prenatal period poses many challenges to the parents and the professionals involved in the process. In addition, counseling sessions can begin earlier to prepare the parents for the complex treatment strategies (Jones, 2002). A similar approach has recently been suggested in the United Kingdom (Cockell & Lees, 2000). Craniofacial treatment programs are available to the parents, and they are increasingly referred to these centers once CLP is diagnosed. These parents represent a challenge to the health care professionals due to their accustomedness to the issue and the inherent problems associated with it (Cockell & Lees, 2000). The severity of CLP and associated malformations are usually incomplete. The couple might choose not to continue the pregnancy, and this can present a challenging situation for the healthcare professionals (Cockell & Lees, 2000). At present, between approximately 14 and 25% of CL, with or without CLP, is diagnosed during the prenatal period. Therefore, this allows for a strategy for prenatal counseling when CLP is detected. Technological advancement and improvement in ultrasonography techniques are likely to increase the number of clefts identified prenatally (Cockell & Lees, 2000). Therefore, an improved awareness regarding the causative factors such as the genetic and environmental factors will provide better tools to approach the etiologic diagnosis, and treatment teams have much to offer families. However, it is critical for those involved in this area to be aware of the potential pitfalls of prenatal diagnosis so that families receive as accurate information as possible (Jones, 2002). All these treatment strategies are only possible if the prenatal care is initiated early.

According to the United States Department of Health and Human Services [USDHHS] (2009), prenatal care awareness created a significant impact during1980s and, due to this there was an increase in the number of women who received their first prenatal visit early during the first quarter of their pregnancy (Simpson, 2011). However, the rate of recent prenatal care during the first quarter decreased in 1990s, that is, from 76.3% in the 1980s to 75.8% in the 1990s (USDHHS, 2009). Furthermore, the rate increased to 83.2% in 2000 and reduced to 67.5% in 2007 (USDHHS, 2009). The researchers showed that there is the wide difference in the percentage of pregnant women participating in prenatal care and that percentage varies widely throughout the United States. This is supported by the fact that in Virginia, a delayed or no prenatal care was obtained in women for a total of 3,628 (3%) and 3,579 (4%) in 2008 and 2009 correspondingly (Annie E. Casey Foundation, 2009b). However, when compared to neighboring states such as North Carolina, delayed or no prenatal care was received in women for a total number of 3,730 (3%) and 3,013 (2%) in same years, respectively. The researchers also indicated prenatal care was the significant factor along with the general good health of the mother to have a healthy newborn infant.

Researchers proved that several risk factors such as maternal age, marital status, education level and occupation play a significant role in identifying women who are at elevated risk for pregnancy complications which could lead to adverse birth outcomes and congenital anomalies (Anya et al., 2008). Technological advancement has reduced the development of these poor health outcomes to a certain extent (Anya et al., 2008). However, some women continue to have adverse pregnancy outcomes due to lack of proper education level, age, occupation, income, religion, and cultural beliefs. These risk factors, in turn, will prevent women from seeking antenatal care during pregnancy resulting in adverse pregnancy outcomes. It has been reported that seeking early prenatal care during pregnancy and the information obtained during prenatal care will increase the chances of having a successful pregnancy and a healthy child (Anya et al., 2008).

Maternal Income, Cleft Lip, Palate, and Admission to NICU

Researchers have identified that OFCs are associated with a low SES of the mother. Therefore, it increases the probability of admission to the Neonatal Intensive

Care Unit (NICU), which increases healthcare cost. OFCs are common birth anomalies that may create considerable burden on the quality and health of the individuals and socioeconomic welfare of the affected person and their families (Wehby & Cassell, 2010). There is a substantial increase in healthcare cost and needs that are associated with it (Wehby & Cassell, 2010). The impact of OFCs and knowledge of their outcome is vital to recognize the unmet needs of the population and creating public policies that decrease the burden on oral cleft at the individual, family, and societal levels. The researchers who conducted a recent study indicated there is an impact of CLP and its outcomes with an emphasis on the length of stay in the NICU, quality of life, quality of health in the long-term, and the use of healthcare as well as its costs and socioeconomic issues (Wehby & Cassell, 2010). Therefore, the researchers recommended future studies on this topic will be critical (Wehby & Cassell, 2010). Additional researchers indicate that oral clefts are one of the birth anomalies that are occurring worldwide and the presence of OFCs require multifaceted medical intercessions and add substantial encumbrance on the quality of life and social life of the individuals and the affected families (Mossey, Little, Munger, Dixon, & Shaw, 2009). Although, the long-term effects of CLP on the health of the individuals and the affected families is still unknown, researchers identified the impact oral clefts have on affected children and hospitalizations throughout their lifetime. Additionally, the more severe forms of the cleft lip have a more profound impact on the additional hospitalizations (Mossey et al., 2009). Researchers indicate that the hospitalization risk of individuals with oral clefts is higher than the general population during their lifetime (Mossey et al., 2009). Through additional research, researchers found that prenatal counseling and feeding instructions were given to parents with cleft lip and palate in many institutions throughout United State (Hubbard, Baker, & Muzaffar, 2012). The study was conducted to identify the effect on children born with CLP and their subsequent admissions to NICU solely for feeding (Hubbard et al., 2012). In the study, parents who received counseling were compared to those who did not receive advice. Ten percent of infants whose parents received counseling were admitted to the NICU with issues associated with feeding alone as compared to 21% of those in the non-counseling group (Hubbard et al., 2012). Therefore, the researchers concluded that prenatal counseling and nursing coaching seems to reduce NICU admissions and stays and alleviate health care costs (Hubbard et al., 2012).

Mossey et al. (2009) suggested there are two groups of CLP, isolated cleft palate and cleft lip with or without cleft palate, which represent varied group of complaints that affect the oral cavity as well as the lips. CL and CLP have a complex effect on speech, hearing, appearance, and psychological issues that lead to lifelong adverse effects on health and social assimilation. Children with these anomalies require comprehensive healthcare from the time they are born until adulthood (Mossey et al., 2009). The mortality rate of children born with this birth anomaly is higher throughout their lifespan than those who are unaffected. However, in developing countries, while the access to healthcare has increased substantially during the recent years, the quality of care varies considerably (Mossey et al., 2009). One primary strategy for controlling the development of this birth anomaly is to prevent the causative factors. The researchers concluded that the technological advances in international collaborations produced some successes in controlling this anomaly (Mossey et al., 2009).

A study was conducted in Japan to examine other anomalies related to CLP and NICU admissions as well as other non-NICU facilities to determine whether there was any difference in admission to NICU versus non-NICU (Koga et al., 2016). The study was conducted in regional facilities as well as nationally in NICU facilities. The regional survey was conducted between 2004 and 2013; however, the national research investigated oral surgery, plastic surgery, and obstetrics and gynecology facilities beginning in 2000 (Koga et al., 2016). According to the national survey the incidence of CL, CLP, and CP per 10,000 births was 4.2 and 6.2% respectively, and according to a regional survey, the rate of CLP and CP were 6.3 and 2.9 respectively (Koga et al., 2016). The researchers concluded that the associated anomalies were significantly higher in the NICU facilities which were similar to international epidemiological study findings. In addition, the obstetric services had the same related anomalies. Therefore, the researchers concluded that incidence of CLP is not different in any facilities whether they are NICU facilities or non-NICU facilities; however, the care and the treatment, investigations on associated malformations, and detailed examinations are more thoroughly performed in NICU facilities (Koga et al., 2016).

Researchers conducting a study in Nigeria found that maternal obesity has a negative impact on their offspring causing them to have fetal anomalies such as CLP, congenital heart defects, neural tube defects (Correa, & Marcinkevage, 2013). Additional researchers who conducted a study on CLP among 14 European countries between 1980 to 2000, including 23 registries and 6 million births, discovered that there are approximately 3,860 CL/CLP cases (70.8%) occurred as isolated anomalies, and 1,589 (29.2%) of the cases were associated with other congenital anomalies such as anomalies of unknown origin, chromosomal anomalies and other syndromes (Calzolari et al., 2007). Accompanying anomalies were more common in newborns who had CLP (34.0%) as compared to infants with CL only (20.8%). The researchers concluded that other anomalies such as musculoskeletal, cardiovascular, and central nervous system defects are typically associated with CLP. The researchers suggested healthcare professionals should take necessary steps to identify structural brain anomalies in patients with CLP for proving clinical management and rehabilitation (Calzolari et al., 2007). Additional researchers found that there are similar negative impacts of maternal obesity on newborns such as high rate NICU admissions with omphalocele, cleft lip, macrosomia, shoulder dystocia, and stillbirth (Ojiegbe, 2016). Another study was conducted in Nigeria to determine the effect of obesity on the childbearing women's health and the necessity of enhancing the awareness among these women. The articles for review in this study include data collected from textbooks, original and online journals, and published reports. The researchers showed that obesity is considered an emergent ailment due to westernization and adoption lifestyle that is unhealthy. The adverse events of obesity include babies born with CLP, neural tube defects, and increased admission to neonatal intensive care units (Ojiegbe, 2016). The researchers determined that although obesity is a preventable problem and management measures are available, women need to be educated on various lifestyle aspects and management measures to control infertility for a better maternal and neonatal outcome (Ojiegbe, 2016).

Methodologies Used in Previous Studies

A literature review was conducted in most of the previous studies. There were differences as well as similarities in methodologies that were used to answer the research questions posed by the researchers. The literature review served to ascertain and link articles that were appropriate to this study, identify the existing gaps in the research and to identify the differences that this research study will discover. The literature review assisted me in determining the different methodologies used by the researchers, and many of the researchers accomplished logistic regression analyses for their research studies. However, it is interesting to note that the methods varied. For instance, to address the smoking association around CLP, estimated a pooled logistic regression of individual-level data, controlling for study fixed effects and individual-level risk was used (Wehby et al., 2017). In another study, the researchers used multiple logistic regressions to estimate unadjusted and adjusted associations with a 95% confidence interval and p-values (Angulo-Castro, 2017). Wehby (2017) found a clinically relevant increase in smoking-related cleft risk among heavier women. But Li et al. (2012) also discovered some associations that were most robust to the development of CLP that includes lack of consuming folic acid during pregnancy, lack of vitamin supplementation during pregnancy, smoking during pregnancy and excess alcohol use in pregnancy. However, in a Mexican study, the main risk factors that are linked to the formation of CL and CP were smoking, alcohol abuse, and a patient's lack of folic acid and multivitamin supplementation during pregnancy (Angulo Castro, 2017). Both the studies used multiple logistic regression to answer the research question. In another study to evaluate a role of these risk factors bivariate analysis was conducted at the first stage of the study. Odds ratio (OR) was calculated for each element, the significance of the results was evaluated by calculating 95% confidence intervals (95% CI). At the next stage of the study, the factors that significantly correlated with the development of orofacial clefts were identified, and multivariate analysis was performed using multiple logistic regression models. The researchers showed that stressful situations among children of pregnant women play an essential role in the formation of CLP (Chincharadze, Vadachkoria, & Mchedlishvili, 2017). Some studies also used qualitative data. Later, in the literature review, it was noted that to observe the relationship between maternal tobacco use and non-syndromic orofacial clefts in newborns, a meta-analysis was conducted using qualitative data (Little, Cardy, & Munger, 2004). Overall, most studies conducted on congenital disabilities were found to be quantitative using similar methodology answer the research questions. Therefore, I believe it is appropriate to use a similar method that was used by other researchers for identifying the association of maternal risk factors to OFC.

Summary

In summary, several risk factors have been identified for the birth anomalies CL and CP. It is necessary to determine the importance of some of the elements that are directly or indirectly linked to CLP to understand whether the incidence rate increasing or decreasing among US population. Although, several risk factors have been identified in the previous studies, it has not been determined if a meaningful relationship among CL and CP and maternal risk factors such as tobacco intake, prenatal care, education, illness, and social demographic factors exists. The result of the literature search showed that there is a gap in the literature and there are inconsistencies in the literature. Since the exact information is not readily available to healthcare professionals, it is possible that the clinicians focus on the incorrect risk factors to lower the occurrence of CLP in the United States. Provision of some definite associations could enable healthcare providers to be aware of the work that is needed to lower the congenital anomaly rates. Due to a significantly increasing population in the United States over the years, there is a necessity to recognize whether these risk factors are affecting the entire community and to determine methods to reduce risk factors. Moreover, literature review identified certain specific gaps in the literature, and concluded that maternal risk factors that are most pervasive were education, age, race/ethnicity, marital status, tobacco use, alcohol use and prenatal care. Therefore, the present study on maternal risk factors could fill the gap in the literature by addressing the etiological factors that contribute to the risk of CLP.

Chapter 3: Research Method

Introduction

CLP is a common birth defect among children in the United States and worldwide. Lack of awareness about the causative factors and preventive measures has created barriers to the reduction of CLP prevalence among women. The purpose of this quantitative, descriptive, non-experimental study was to determine if there is a relationship between CLP and maternal characteristics such as reproductive history (advanced maternal age, maternal obesity, number of prenatal visits, month prenatal care began, number of pregnancies, gestational age at birth, assisted reproductive technology used, gestational diabetes, and gestational hypertension), socioeconomic status of the mother (marital status, education, mother's race, payment source for delivery, and place where birth occurred), and admission to the NICU in U.S. hospitals from January 2016 through December 2016. In this chapter, I discuss research design and methods, target population, sampling procedures, instruments, data collection procedures, and data analysis. I also explain the reliability, validity, and ethical procedures of the study.

Research Design and Rationale

In this cross-sectional, quantitative study I used secondary data from the NCHS National Vital Statistics System's Natality data set. I used quantitative design to assess multiple variables and test the hypotheses (see Creswell, 2009). The quantitative methodology also allowed me to measure any association between the different potential risk factors and CLP; I analyzed the results of this research using mathematically-based methods (Aliaga & Gunderson, 2002). This chosen quantitative design allowed me to collect the data from a specified timeframe (see Merrill & Timmreck, 2006).

The cross-sectional study design entailed examining not only the association between the disease of interest and risk factors of a target population over a short period of time, but also assessing the frequency as well as the burden of illness of a community at a given point in time (see Public Health Action Support Team [PHAST], 2011). Epidemiologists have used cross-sectional study designs to assess the association of risk factors with health outcomes of interest over an extended period (PHAST, 2011). In particular, epidemiologists have used cross-sectional designs to understand the distribution of disease in target populations and to make comparisons of disease occurrence between population groups (PHAST, 2011). Therefore, cross-sectional design serves as a useful measure to advance knowledge in epidemiology. I did not expect time and resource constraints as issues because the merits of cross-sectional study design allowed me to conduct the research relatively quickly and easily (see PHAST, 2011).

I first used a descriptive quantitative analysis to identify each maternal risk factor such as maternal obesity, advanced maternal age, and reproductive history individually in the data set. I then conducted a logistic regression analysis to determine if there was a relationship between the independent variables and the dependent variable. The study's independent variables were maternal demographics, maternal biological factors, maternal reproductive history and admission to NICU; the dependent variable was CLP.

Methodology

Population

I used a secondary dataset from the birth records database for the year 2016. The target population for this study was U.S. resident women who gave live birth to infants. The data obtained contains all births registered within all U.S. states. It is important to note that more than 99% of births occurring in this country are registered (NCHS, 2016). The CDC maintains national birth surveillance information from case report forms submitted by individual state and local health departments. Birth certificate data is annually updated, and the most recent raw data is for the year 2016. The study population included women who gave live births to infants in the United States. In 2016, the vital statistics department registered 3,945,875 births, a rate that had decreased 1% from the 2015 data. The dataset provides enough participants to identify many characteristics of women associated with CLP occurrence in the United States. Therefore, the sample size was determined using the inclusion criteria from the 3, 945,875 births that occurred in 2016.

Sampling and Sampling Procedures

Sampling refers to the method researchers use during data collection to improve the accuracy, quality, and homogeneity of data. Sampling is essential to make inferences about the target population. A study's generalizability depends on the representativeness of the sample a researcher uses to help make assumptions about a target population (Frankfort-Nachimias & Nachimias, 2008). A sampling strategy, in turn, may enhance the generalizability of the sample to the community of interest (Crosby, DiClemente, &

Salazar, 2006). Leveraging a representative sample helped me ensure integrity of my inferences about the population and gave credibility to the study's overall scientific findings. With this in mind, I used secondary data collected in the CDC's WONDER to produce a representative sample of the target population (CDC, 2016). WONDER is an Internet system that makes the CDC's information resources available to public health professionals and the public at large.

I used purposive sampling to select the study population and to collect data to answer the research questions. Pregnancies resulting in CLP infants were identified from the birth certificates data base. I limited samples to the birth records of women who gave live birth to infants. The data was collected by the public health departments of each state and compiled by the vital statistics department for all births that occurred in the United States. Although the birth certificate data contained the entire female population who delivered live births in the United States, the sample was not representative of the entire U.S. population because it did not include data from U.S. residents who had live births outside United States. Live births in 2016 included 3,945,875 participant's birth records that contained information for maternal risk factor on CLP.

This research was grounded in data from the Natality data file from the National Vital Statistics System (NVSS). The vital statistics data was based on information derived from birth certificates and included information for all births occurring in the United States. The birth records came from women who gave birth to infants in the United States between January 2016 and December 2016. The CDC also checks the data for accuracy and completeness of the birth records (CDC, 2015e). In this study, I only used data from fully-completed birth records. The data were filed and organized based on each delivery performed, and each state was federally required to file the data (CDC, 2015e). All 50 states, New York City, the District of Columbia, and all U.S. territories report birth record information to the CDC's NCHS in a standard format (CDC, 2015e). Although the birth certificates were not entirely standardized for all reporting areas, they all contained the core information required for reporting to the NCHS; this included maternal demographic characteristics, pregnancy history, infant characteristics, and medical risk factors (Martin, Hamilton, Osterman, Driscoll, & Drake, 2018).

The sampling frame consisted of all U.S. counties in all 50 states, including the District of Columbia. The inclusion criteria guaranteed that all states in the U.S. and District of Columbia were included, accounting for defined geographic areas, appropriate proportions of minority populations, and proper proportions of age, ethnic, and income groups (CDC, 2013b). The inclusion criteria for the study was based on birth certificates being completed by (a) women who lived in the United States from January 2016 to December 2016, (b) women who had a live birth anytime from January 2016 to December 2016, (c) and women who provided precise birth certificate information for their infants to the regional vital statistics office. The exclusion criteria included women (a) who were U.S. nationals residing outside of the United States between January and December of 2016, (b) who did not have a live birth, (c) and who did not provide complete information on the birth certificate for their infants.

The sample characteristic that I selected included birth records that were completed by women who gave birth in 2016 to infants who were alive at birth. The infant's birth certificate information had to be accurately provided to their respective state's public health department. The vital statistics office collected data on all women in the United States who had a live birth. This data was publicly available.

Power Analysis

I used G*power Version 3.1 software to calculate the sample size, using logistic regression as the statistical test method. The input parameters were those for a priori analysis: computer-required sample size-given α, power and effect size, model *z* tests, two-tailed logistic regression, and the statistical significance level set at $\alpha = 0.05$. The effect size provided an estimate of strength of the association between both the dependent, independent, variables in this study. The power (*1-β err prob.)* was set at 0.80 or (80% CI); this was the probability of estimated participants assumed to be sufficient enough to find statistical effect size of 0.3% or (30%), anticipated *OR* significance of 1.3, and R^2 or other X = 0.90. *Pr (Y = 1/X = 1) H0* = 0.2. The calculated sample size was 721.

Procedures for Data Collection

I conducted a retrospective study using secondary data obtained from the CDC vital statistics birth certificate records. These provided the most comprehensive information to fulfill the study objectives and answer the research questions. The existing data had many collected variables and had information about women who gave birth to live infants in the United States (CDC, 2017). Moreover, my use of secondary data was the most time and cost effective method and also allowed me to examine a wide variety of variables and their relationships since there was no data collection nor follow up required from the patients. The data was also readily available to the public for analysis, and I needed no other Institutional Review Board (IRB) approval other than that from the Walden University's IRB (see Creswell, 2014; Frankfort-Nachmias & Nachmias, 2008). Secondary data from NVSS also served as an ideal data set for this study because they provided sufficient sample size to answer the research questions (see CDC, 2017; Frankfort-Nachmias & Nachmias, 2008).

The NCHS houses and provides public access to complete health statistical records collected from all 50 states. I used the birth data to assess the birthing population within the United States, using birth certificate data collected by the NCHS. The NCHS developed the birth certificate data collection tool, which was most recently revised in 2003 (NCHS, 2006). There was no need to ask permission to use these instruments since the data collected using the instruments were publicly available. Instruments used in birth certificates were unique to the birth certificate form to obtain health-related data from the U.S. population.

I downloaded the NVSS data in an excel spreadsheet, then transferred them to SPSS. I examined maternal risk factors existing among the U.S. population using data collected by the NCHS. To ensure consistency, data base used standardized birth certificate forms. The NCHS (2001) ensures that the standardized certificates meet current needs by periodic reviews and revisions that occur on a 10 to 15-year cycle. The birth certificate form is shown in Appendix A.

The Natality data set was provided by the NCHS. In the United States, state laws require birth certificates to be completed for all births, and federal law mandates national collection and publication of births and other vital statistics data. The NVSS is the result of the cooperation between the NCHS and the 50 states to provide access to statistical information from birth certificates. The birth certificate is usually completed by parents with the help of hospital staff after birth of the baby and is entered into electronic birth registration (EBR) systems.

The EBR consists of systems designed for freestanding software in birthing facilities. The software captures the data, carries out limited editing, and transmits data to the state for further processing (NCHS 2016). The birth certificate information is then filed with the state's vital records office. State processing is then executed with software developed by the same vendor who developed the facility software or by using software developed by the state staff. A system housed and operated centrally at the state office may facilitate system maintenance, version control, security, and uniform processing of data.

It is recommended that each state-operated EBR input system replicates the data input system used by the facilities and providers in the field. The NCHS (2016) will review state software for the handling of data elements to ensure that the data are collected and recorded as intended. The EBR specifications were developed assuming the NCHS standard worksheets. The data will be sent to NCHS as soon as possible after receipt and initial processing by the state. The state shall not wait for the results of queries before transmitting a record. Additional queries and updates are forwarded to NCHS as soon as the updated record is accepted by the state (NCHS 2016).

Various raining materials were prepared on each of the certificates and reports and were directed at specific individuals responsible for completing vital records. Information on how the registration system operates, item-by-item instructions for completing each item and rationales for collecting the information were included (NCHS 2016). Materials were produced by NCHS and provided detailed guidance on completion of vital records, as well as procedures involved in the classification, coding, and processing of data collected from vital records. The NCHS produces a variety of instruction manuals to aid mortality medical coders, sociologists, and other individuals responsible for processing vital records. These manuals are used by both state vital statistics programs and the NCHS (NCHS 2016).

The birth certificate data for 2016 marks the first year in which data for all 50 states and the District of Columbia (D.C.) are included in the data based on the 2003 revision of U.S. Standard Certificate of Live Birth. Certain items like tobacco use during pregnancy, usage and timing of prenatal, which are the independent variables of this study, were not previously included but were included in 2016 data. However, the file for geographic information was not available for public use but can be available upon special request. Birth data may also be accessed via the Centers for Disease Control and Prevention's online data portal known as WONDER.

Operationalization of Variables

The birth records from National Center Health Statistics (NCHS) department provided the data for mothers who delivered live births from January to December 2016. Following is a description of the dependent and independent variables.

The dependent variable was the presence of CL cleft lip with or without CP. The independent variables includes maternal reproductive history (maternal age, maternal body mass index [BMI]), socioeconomic status, marital status, education, mother's race, payment source for delivery, and place where birth occurred), number of prenatal visits, commencement of prenatal care, number of pregnancies, gestational age at birth, use of assisted reproductive technology, gestational diabetes, gestational hypertension, and admission to the NICU.

Table 1

Variable Descriptions

Variable type	Code	Level of Measurement	Values
Maternal age	MAGER9	Categorical (Ordinal)	1=under 15 years 2=15-19 years 3 =20-24 years 4= 25-29 years 5= 30-34 years 6=35-39 years 7=40-44 years 8=45-49 years 9= 50-54 years
Number of prenatal visits	PREVIS_REC	Categorical (Ordinal)	01= No visits 02=1 to 2 visits 03= 3 to 4 visits 04 = 5 to 6 visits 05=7 to 8 visits 06=9 to 10 visits 07=11 to 12 visits 08=13 to 14 visits 09=15 to 16 visits 10=17 to 18 visits 11= 19 or more visits 12 =unknown or not stated

Variable type	Code	Level of Measurement	Values
Month prenatal care began	PRECARE5	Categorical (Ordinal)	1=1st to 3rd month 2= 4th to 6th month 3=7th to final month 4= No prenatal care 5= Unknown or not stated
Number of pregnancies	TBO_REC	Categorical (Ordinal)	1-7= Number of total birth order 8= 8 or more live births 9= Unknown or not stated
Gestational age at birth	OEGest_R3	Categorical (Nominal)	1= under 37 weeks 2= 37 weeks and over 3= not stated
Use of assisted reproductive technology	RF_ARTEC	Categorical (Nominal)	Y= Yes N= No X= Not applicable U= Unknown or not stated
Gestational diabetes	RF_GDIAB	Categorical (Nominal)	Y= Yes N = No U = Unknown or not stated
Gestational hypertension	RF_GHYPE	Categorical (Nominal)	Y= Yes N = No U = Unknown or not stated
Admission to NICU	AB_NICU	Categorical (Nominal)	Y= Yes N = No U = Unknown or not stated

Variable type	Code	Level of Measurement	Values
Mother's Race	MBRACE		1 = White 2 = Black 3 = American Indian or Alaska Native 4 = Asian or Pacific Islander
Mother's Marital status	DMAR		1 = Married 2 = Unmarried
Mother's Education	MEDUC		1= 8th grade or less 2= 9th grade through 12th grade with no diploma 3=High school graduate or GED completed 4=Some college credit but no a degree 5=Associate degree (AAS) 6=Bachelor's degree (BA, AB, BS) 7=Master's degree (MA, MS, Meng, Med, MSW, MBA) 8=Doctorate (PhD, EdD or professional degree) 9=unknown
Payment source for Delivery	PAY_REC		1=Medicaid 2=Private Insurance 3 =Self Pay 4= Other 5= Unknown
Place where birth Occurred	BFACIL3		01= In Hospital 02=Not in Hospital 03= Unknown or not stated

Mother's pre-pregnancy body mass index (BMI)

BMI provided an indication of the mother's body fat based on her height and pre-pregnancy weight. Mother's pre-pregnancy BMI is calculated as: [mother's pre-pregnancy weight (lb) / [mother's height (in)]2] x 703.

Advanced maternal age

The age of mother was derived from the reported month and year of birth. Age of mother was imputed for ages 8 years or under and 65 years and over (mother's age 9 years was recoded as 10 years and ages 55-64 years are recoded to an age from 50-54 years). Births from mothers aged 9-11 years were collapsed into the categories "12 years or under;" births from mothers aged 50-64 years were categorized into "50-54 years."

Number of prenatal visits

Information on the timing and number of prenatal care visits was collected from the item "Date of first prenatal visit" (with a checkbox for "No prenatal care") and "Total number of prenatal visits for this pregnancy." The public use file included the month prenatal care began (ranging from months 1-10 of the pregnancy based on the obstetric estimate of gestation) as well as a recode for the trimester prenatal care began (1st, 2nd, or 3rd).

Month prenatal care began

This denoted the gestational age at which the prenatal care began.

Number of pregnancies (Total birth order)

Live-birth order and parity were determined from two items on the birth certificate, "Number of previous live births now living" and "Number of previous live births now dead." Live-birth order and parity classifications referred to the total number of live births the mother has had including the 2016 birth.

Gestational age at birth

Births occurring before 37 completed weeks of gestation were considered preterm for purposes of classification consistent with the ICD-9 and ICD-10 definitions. NCHS further categorized births at less than 34 weeks as early preterm and births at 34-36 weeks as late preterm. Births occurring between 37 and 38 completed weeks were considered early term, between 39 and 40 completed weeks as full term, 41 completed weeks as late term, and at 42 completed weeks and over as post-term. These distinctions were consistent with the revised American College of Obstetrics and Gynecology revised term definitions (American College of Obstetricians and Gynecologists [ACOG], 2013).

Assisted reproductive technology (ART) utilization (Pregnancy resulting from infertility treatment)

ART procedures are those in which both egg and sperm are handled in the laboratory. Assisted reproductive technology includes in vitro fertilization (IVF), and gamete/zygote intrafallopian transfer (GIFT, ZIFT).

Gestational diabetes mellitus (GDM)

This variable refers to diabetes diagnosed during pregnancy; Gestational diabetes mellitus (GDM) can be IDGDM–Insulin dependent gestational diabetes mellitus, Class A1 or A2 diabetes mellitus.

Gestational hypertension

This variable refers to hypertension diagnosed in pregnancy (pregnancy-induced hypertension or preeclampsia). Gestational hypertension can be pregnancy-induced hypertension (PIH), preeclampsia, eclampsia, transient hypertension and HELLP syndrome.

Admission to the NICU

The admission of the newborn to the neonatal intensive care unit was reported as Yes, No, Unknown, or Not Stated.

Mother's marital status

It is recommended that information on marital status be reported directly by the mother using the Mother's Worksheet. In the birth certificate data, the mother's marital status was obtained exclusively by a direct question in the Mother's Worksheet and was then imputed for the birth certificate records. If status was not recorded on the worksheet and unknown but the father's age was known, then the mother was recorded as married. If the status was unknown, and the father's age unknown, then the mother was recorded unmarried.

Mother's education

Educational attainment was based on the highest degree or level of school completed at the time of the delivery. It was recommended that information on educational attainment of the mother be reported directly by the mother using the Mother's Worksheet.

Mother's race (Bridged Race Mother)

Bridged race included individuals reporting only one race and individuals reporting more than one race bridged to a single race. The five categories for race specified in the revised standards are: American Indian or Alaska Native (AIAN), Asian, Black or African American, Native Hawaiian or Other Pacific Islander (NHOPI), and White. Where race of the mother was not reported, if the race of the father was known, the race of the father was assigned to the mother. When information was not available for either parent, the race of the mother was imputed according to the specific race of the mother on the preceding record with a known race of mother.

Payment source for delivery

There were four options for source of payment at delivery that were identified in a checkbox format: 1) private insurance; 2) Medicaid; 3); self-pay; and 4) other (must be specified). If the item was not completed (i.e., none of the boxes are checked), it was classified as “Not stated.” The instructions were to check the box that best described the principal source of payment for this delivery. If “Other” was checked, the payer was either specified or entered as “unknown.”

Place where birth occurred

Five options for place of birth were identified in a checkbox format: 1) hospital; 2) freestanding birth center; 3) home birth, 4) clinic/doctor’s office and 5) other (must be specified). If the item was not completed (i.e., none of the boxes are checked), it was classified as “Not stated.” It was recommended that this information be collected directly from the medical record using the Facility Worksheet. It was again recoded as birth occurred in hospital, out of hospital, and unknown or not stated.

Data Analysis Plan

The data file for 2016 birth certificate file was released in Excel format and was converted into SPSS format using SPSS software version 21 for analysis of data relevant to the current study. SPSS is an appropriate software to use for analysis since the software is capable of storing large amounts of data and the variables can be easily coded and re-coded; identifying the variables and labeling was also possible in the variables section. To test the hypotheses and answer the research questions, I conducted logistic regression analyses to identify the relationship between maternal risk factors and CLP among U.S. women. The use of logistic regression was appropriate to analyze statistically significant characterization between multiple variables (Shuttleworth, 2008).

Each of the variables used in this study resulted from the birth certificate questionnaire that provided quantitative, categorical results. I used SPSS version 21 to perform logistic regression analyses. I accounted for missing data by using the SPSS option of “missing cases.” Because I de-identified the data, correction or imputations of discrepant data were are not an option. Data cleaning and screening procedures included: 1) Ensuring that the values of data were credible (Issel, 2009) 2) Ensuring that there was no data entry error in the Natality dataset, executed through the means of 3) Screening the plausibility of amounts of data (Issel, 2009). I screened the data for outliers and excluded any outliers by determining cut-off points and using a large sample size to lessen its effect on data analyses (Issel, 2009). The main purpose of the study was to identify the status of the risk factors and the relationship between the independent and dependent variables; therefore, it was appropriate to conduct a descriptive statistic as well as logistic regression.

The study was guided by the following research questions and hypotheses:

RQ1: Is there a significant relationship between cleft lip and cleft palate birth defects and maternal reproductive history (maternal age, maternal obesity, number of prenatal visits, month prenatal care began, number of pregnancies, gestational age at birth, assisted reproductive technology used, gestational diabetes, gestational hypertension) among mothers who delivered live infants in U.S. hospitals and birthing centers from January 2016 to December 2016?

$H_0$1: There is no significant relationship with cleft lip and cleft palate birth defects and maternal reproductive history (maternal age, maternal obesity, number of prenatal visits, month prenatal care began, number of pregnancies, gestational age at birth, assisted reproductive technology used, gestational diabetes, gestational hypertension) among mothers who delivered live infants in U.S. hospitals and birthing centers from January 2016 to December 2016.

$H_1$1: There is a significant relationship with cleft lip and cleft palate birth defects and maternal reproductive history (maternal age, maternal obesity, number of prenatal visits, month prenatal care began, number of pregnancies, gestational age at birth, assisted reproductive technology used, gestational diabetes, gestational hypertension) among mothers who delivered live infants in U.S. hospitals and birthing centers from January 2016 to December 2016.

RQ2: Is there a significant relationship between socioeconomic status of the mother (marital status, education, and mother's race, payment source for delivery and place where birth occurred) and CLP resulting in admission to the NICU (indicating high health care cost) in U.S. hospitals from January 2016 to December 2016?

$H_0$2: There is no significant relationship between socioeconomic status of the mother (marital status, education, and mother's race, payment source for delivery and place where birth occurred) and CLP resulting in admission to the NICU (indicating high health care cost) in U.S. hospitals from January 2016 to December 2016?

$H_1$2: There is a significant relationship between socioeconomic status of the mother (marital status, education, and mother's race, payment source for delivery and place where birth occurred) and CLP resulting in admission to the NICU (indicating high health care cost) in U.S. hospitals from January 2016 to December 2016.

I used descriptive statistics to report information about each of the variables in Table 1. The reporting of descriptive statistics included frequencies (distribution and percentages), mode, mean, range, and median. For research questions 1, and 2, for identifying the association between dependent variable (CLP) and independent variables (maternal risk factors), I used binomial logistic regression. Binomial logistic regression was appropriate when the dependent variable outcome was dichotomous (yes/no) and more than one categorical or (ordinal), and or when either dichotomous or continuous variables were present. It can be used to estimate the association between one or more variables. Chi-square test was used to test the hypothesis when the two attributes (categorical variables instead of quantitative variable) were independent or when there was no significant association between the two attributes. Binary logistic regression was used to make direct relationship between dependent and independent variables. The significance level (α) was set at 0.05 to denote statistical significance with a confidence interval (CI) of 95%. Using the *p*-value approach, statistical significance would be determined in such way that $p<0.05$ would indicate the null hypothesis can be rejected and the result was statistically significant.

Threats to Validity

When research is valid, the conclusions drawn by the researcher are legitimate. Unfortunately, there are many threats to the validity of research, and these threats may sometimes lead to unwarranted conclusions. Validity is not an all-or-nothing proposition, which means that some research is more valid than other research. Only by understanding the potential threats to validity will one be able to make knowledgeable decisions about the conclusions that can or cannot be drawn from a research project.

Creswell (2009) and Frankforth-Nachmias and Nachmias (2008) assessed that there are two types of threats to validity: internal and external validity. Internal validity implores that research be constructed so as to eliminate the possibility that factors other than those being investigated are responsible for changes in the dependent variables. Therefore, to establish internal validity, a researcher must be able to answer whether the change in independent variable was responsible for the change in dependent variable. Internal validity often occurs at the onset of research operation (Frankforth-Nachmias & Nachmias, 2008). External validity is threatened when researchers draw incorrect inferences from sample data. It also occurs when findings are generalized to larger populations and applied at different settings either in the past or to relevant future studies. It is therefore, possible that threats to validity occur during the course of the study, especially when conducting the research, during data analysis, and during interpretation of results (Creswell, 2009).

There are certain limitations and data assumptions in retrospective data for using the secondary data. Threat to validity can be affected by having to work with a high percentage of missing data in the file and the researcher having no control of this. The presence of missing values will have a great impact on the statistical analysis and the results obtained. Additionally, most of the answers to the pregnancy questions in the data were self-reported and self-recalled, one can only assume that patients accurately recollected the history of pregnancy and that accurate information was reported while answering the questions.

Creswell (2014) and Frankfort-Nachmias and Nachmias, (2008) reported that while cross-referencing with other related variables is a method to identify he reliability and validity of the self-reported problems, there can also be problem with the misinterpretation of the questions in self-reported data, and this can be a threat to the validity of information. The anonymous and voluntary nature of participation in research study intrinsically increases the likelihood of honest responses provided by participants. My research assumed that honesty shall prevail to reveal an objective reality. External validity can be described as the extent to which the study findings can be generalized to target population (Crosby, DiClemente, & Salazar, 2006).

Ethical Procedures

The data used in this study was publicly available, and the privacy of participants was protected by public law while the data collected using the survey was kept strictly confidential (CDC, 2016). The data was de-identified and anonymous. I had obtained Walden University IRB approval before initiating the study. The laptop that I used for storing data in the survey was password protected, and I was the only one who had access to the computer. Data shall be destroyed after five years. With approval from the Walden Institutional Review Board, the information for the study was obtained from the CDC, vital statistics data. The data source was the data from the birth certificates of the women who delivered infants within the United States, and it was collected and compiled by each state's division of public health.

The de-identified data was transferred to the National Vital Statistics System. Although I obtained de-identified the data, I made adequate provisions for protecting the personal identifiers and data protection. The de-identified data will not harm the participants in any way, and I received the data securely in a password-protected laptop. The participants will not experience any risk since I only used de-identified data, and I did not have to contact or collect data from the actual participants.

Once the data was compiled by the National Vital Statistics Department, the information was available to the public through CDC WONDER, therefore no permission was required to obtain this data. No consent form was necessary since it is de - identifiable data. Also, no approval was required from any other institutions other than Walden University IRB. The publicly available data was accessible to anyone who would be interested in an analyzing it.

Summary

In conclusion, this study used a cross-sectional quantitative study design to identify if maternal risk factors such as maternal behavior, maternal reproductive history, and socioeconomic status among others are causative factors to the prevalence of CLP in the United States and admission to the NICU. The research questions were answered using secondary data from the birth certificate by the office of Vital Statistics for the birthing population of mothers in the United States for the year 2016. Chapter 3 explains the research methodology, sample size, data collection, and methods of analysis. Ethical concerns are also discussed in this chapter. Chapter 4 provides results of the quantitative data analysis, which includes descriptive statistical information and binomial logistic regression analysis.

Chapter 4: Results

Introduction

The purpose of this quantitative, non-experimental, cross-sectional study was to investigate the association of CLP and maternal characteristics among women who delivered live births in the United States between January and December 2016. I used a secondary dataset from the birth certificates data compiled by the NCHS and housed in the CDC WONDER. The presence of CL with or without CP was measured as a pregnancy outcome by assessing the status of the baby at birth through the information provided in the birth certificate data.

The following research questions and hypotheses guided this study:

RQ1: Is there a significant relationship between CLP and maternal reproductive history (advanced maternal age, maternal obesity, number of prenatal visits, month prenatal care began, number of pregnancies, gestational age at birth, assisted reproductive technology used, gestational diabetes, and gestational hypertension) among mothers who delivered live infants in U.S. hospitals and birthing centers from January 2016 to December 2016?

$H_0$1: There is no significant relationship with CLP and maternal reproductive history (advanced maternal age, maternal obesity, number of prenatal visits, month prenatal care began, number of pregnancies, gestational age at birth, assisted reproductive technology used, gestational diabetes, and gestational hypertension) among mothers who delivered live infants in U.S. hospitals and birthing centers from January 2016 to December 2016.

*H_1*1: There is a significant relationship with CLP and maternal reproductive history (advanced maternal age, maternal obesity, number of prenatal visits, month prenatal care began, number of pregnancies, gestational age at birth, assisted reproductive technology used, gestational diabetes, and gestational hypertension) among mothers who delivered live infants in U.S. hospitals and birthing centers from January 2016 to December 2016.

RQ2: Is there a significant relationship between socio economic status of the mother (marital status, education, and mother's race, payment source for delivery, and place where birth occurred) and CLP resulting in admission to the NICU in U.S. hospitals from January 2016 to December 2016?

*H_0*2: There is no significant relationship between socioeconomic status of the mother (marital status, education, and mother's race, payment source for delivery, and place where birth occurred) and CLP resulting in admission to the NICU in U.S. hospitals from January 2016 to December 2016?

*H_1*2: There is a significant relationship between socioeconomic status of the mother (marital status, education, and mother's race, payment source for delivery, and place where birth occurred) and CLP resulting in admission to the NICU in U.S. hospitals from January 2016 to December 2016?

In this chapter, methods for data collection will be reviewed; I present the descriptive statistics of the dependent and independent variables, as well as the study covariates. I will also discuss the inferential statistics analysis and hypothesis testing for the research question, the results of the statistical analyses, and provide a summary of the answers to the research questions.

Data Collection

I retrieved birth certificate data ranging from January 2016 to December 2016 that were pertinent to each of the research questions. Prior to data collection, I obtained approval from Walden University's (IRB (#06-04-18-0426589). Following IRB approval of my research proposal, I accessed the data set from the CDC WONDER from January to December 2016.

The CDC Wonder data included all 50 U.S. states and the District of Columbia. The sampling used for the study was purposive and a representative sample of the U.S. population (Martin, Hamilton, Osterman, Driscol, & Drake, 2017). A total of 3,956,112 births were registered in the United States from January to December 2016, a decrease of 1% from 2015. The general fertility rate declined to 62.0 per 1,000 women aged 15–44 as compared with rates in 2015. There was a 9% decline in birth rate for females aged 15–19 in 2016, but there was an increase in births for women in their 30's and early 40's. The total fertility rate declined to 1,820.5 births per 1,000 women in 2016. The birth rate for unmarried women declined, while the rate for married women increased. More than three-quarters of women began prenatal care in the first trimester of pregnancy (77.1%) in 2016, while 7.2% of all women smoked during pregnancy (Martin et al., 2017). The cesarean delivery rate declined for the fourth year in a row. Medicaid was the source of payment for 42.6% of all 2016 births. The preterm birth rate rose for the second straight year, and the rate of low birthweight increased 1%. Twin, triplet, and higher-order multiple birth rates declined, although these changes were not statistically significant (Martin et al., 2017).

Vital statistics and birth certificate data is used by researchers for a variety of purposes, both administrative and scientific. However, despite these purposes, it is not always possible to provide a correct interpretation of this data without considering various qualifying factors and methods of classification. These factors and methods must then be considered in relation to the purposes for which the data is being used. Factors researchers regularly identify as limiting the use of data are related to imperfections in the original records (e.g., missing or misclassified) or that rearranging these data into detailed categories is impractical. While these limitations should not be ignored, they do not necessarily diminish the value of the data and the most general purposes of their interpretation. Furthermore, there were two other factors I considered when evaluating the quality of the data. The first is completeness of registration. More than 99% of all births occurring the in the United States in 2016 were registered. Another factor is completeness of reporting. Another measure of data quality is the “not stated” percentage; I thus interpreted items with a high percentage of “not stated” responses with caution.

The NCHS automatically checks for completeness when it receives electronic files, verifying through individual item code validity and flagging any unacceptable inconsistencies between data items which are then reviewed by staff on a regular basis to identify any issues with the overall data quality (such as inadequate reporting items, failure to follow NCHS coding rules, and systems and software errors). In the past, procedures for quality assurance were traditionally limited to the review and analysis of differences between NCHS and registration area code assignments for a small sample of records.

However, the increased use of EBR has augmented this procedure through analyses of year-to-year and area-to-area variations in the data. The NCHS investigates all differences that they judge to impact the quality and completeness of the data. In this review process, statistical tests are used to flag differences for possible follow-up. As necessary, registration areas are then asked to either verify the counts or to determine the nature of the differences in the contested items. Missing records (except those permanently voided) and other problems detected by NCHS are resolved, and corrections are transmitted to NCHS.

The history of documentation proves that, apart from the most visible and severe cases, congenital anomalies have been under-reported on birth certificates. This under-reporting has been at least partly attributable to the inclusion of anomalies on the 1989 U.S. Standard Certificate of Live Birth. The 2003 revision of the U.S. Standard Certificate attempted to improve this reporting by including only those that were diagnosable within 24 hours of birth using conventional diagnostic techniques. However, as instances of these anomalies were too few to be included in any quality studies, it cannot be clearly determined whether these efforts were successful. I made no changes to the sample size or data collection procedures as explained in Chapter 3.

Any data set will inevitably have missing data (Bhattacherjee, 2012). This is because the respondents may not answer some of the questions, and it is important for the researcher to identify and correct the missing cases before conducting data analysis. Therefore, before starting the data analysis, I screened the data set for any obvious discrepancies and to ensure the data fields were entered correctly. This process enabled me to determine how to handle the missing data, identify any outliers, and assess if there were any violations to the test of assumptions. The results of my analysis showed that there were some missing values were present, but there were no patterns in the missing values and how it is organized. Almost all data (99%) was complete, while 1% of the data had incomplete values. According to Mertler and Vannatta (2013), it is ideal to remove the missing cases or to calculate the mean of the missing value and then replace the missing values before starting the analysis. Descriptive statistics were conducted in SPSS to retrieve the missing values, and I found that the missing cases (n = 6828) accounted for 0.2% of the CLP cases. The incomplete cases were removed from the preliminary analysis before the actual analysis of the data began. Deleting cases with missing data neither changes the overall meaning of the data, nor affects the variance since the number of missing values in the data set were few (Mertler & Vannatta, 2013). However, not all missing data were required to be deleted because I was only interested in certain variables. After having deleted the missing cases from the original total of 3,956,112 U.S. registered births in 2016, the final data set contained 3,949,284 births.

Results

I used descriptive statistics to analyze the demographics of participants in this study, and crosstabs were used to describe the relationship between CLP and each independent variable. Additionally, I describe the binomial regression analysis later in this chapter.

Demographic Variables

This study included 3,949,284 participants. I used SPSS Version 21.0 to generate demographic percentages, frequencies, means, and standard deviation. Tables 2-8 provide descriptive statistics for the study participants

Table 2

Marital Status of Mother

Status	Frequency	Percent
Married	2,379,424	60.2
Unmarried	1,569,860	39.8
Total	3,949,284	100.0

Table 3

Mother's Age

Age range	Frequency	Percent
Under 15 years	2,255	.1
15-19 years	209,894	5.3
20-24 years	804,267	20.4
25-29 years	1,150,217	29.1
30-34 years	1,112,277	28.2
35-39 years	548,012	13.9
40-44 years	113,276	2.9
45-49 years	8,285	.2
50-54 years	801	.0
Total	3,949,284	100.0

Table 4

Mother's Race

Race	Frequency	Percent
White	2,950,105	74.7
Black	653,329	16.5
American Indian or Alaskan native	43,531	1.1
Asian or Pacific Islander	302,319	7.7
Total	3,949,284	100.0

Table 5

Mother's Education

Level of education	Frequency	Percent
9th through 12th grade with no diploma	406,914	10.3
High School graduate or GED completed	979,690	24.8
Some college credit, but no degree	807,864	20.5
Associate degree (AA, AS)	322,258	8.2
Bachelor’s degree (BA, A, BS)	787,416	19.9
Master’s degree (MA, MS, MEng, Med, MSW, MBA)	359,271	9.1
Doctorate (PhD, EdD) or Professional degree (MD, DDS, DVM, LLB, JD)	102,580	2.6
Unknown	51,075	1.3
Total	3,949,284	100.0

Table 6

Number of Maternal Prenatal Visits

Range	Frequency	Percent
No visits	61,870	1.6
1 to 2 visits	45,801	1.2
3 to 4 visits	98,536	2.5
5 to 6 visits	192,287	4.9
7 to 8 visits	360,520	9.1
9 to 10 visits	792,291	20.1
11 to 12 visits	993,571	25.2
13 to 14 visits	682,225	17.3
15 to 16 visits	372,454	9.4
17 to 18 visits	103,727	2.6
19 or more visits	134,955	3.4
Unknown or not stated	111,047	2.8
Total	3,949,284	100.0

Table 7

Payment Source at Delivery

Source	Frequency	Percent
Medicaid	1,668,120	42.2
Private Insurance	1,935,486	49.0
Self-Pay	168,422	4.3
Other	153,622	3.9
Unknown	23,634	.6
Total	3,949,284	100.0

Table 8

Facility Distribution

Facility	Frequency	Percent
In hospital	3,885,870	98.4
Not in hospital	63,212	1.6
Unknown or not stated	202	.0
Total	3,949,284	100.0

Overall, respondents were between age 12 and 55 years, with a mean age of 29 years. A majority of the respondents delivered their babies between the ages of 20-34 years. Married respondents comprised 60.2% of the sample, while 39.8% were single. A majority of the respondent population were white (74.7 %), whereas 16.5% of respondents were black. More than half of respondents (58.9%) had an education below an associate degree, 8.2% had an associate degree, while 19.9% had a bachelor's degree, 9.1% had a master's, and 2.6% had a doctoral degree. Almost half of the sample delivered payment though private insurance (49%), and an almost equal amount had Medicaid (42.2%) as the source of payment for their delivery. A majority of the participants received antenatal care during their last pregnancy as indicated by their prenatal visit (between 9-14 visits), and only 1.6% did not attend prenatal visits while 5.2% attended 1-4 visits.

Descriptive Statistics for Covariates and Cleft Lip and Palate

I analyzed the associations between birth defects such as CLP with the covariates of marital status, education level, mother's race, payment source for delivery, and maternal characteristics such as reproductive history advanced maternal age, maternal obesity, number of prenatal visits, the month prenatal care began, number of pregnancies, gestational age at birth, assisted reproductive technology used, gestational diabetes, gestational hypertension, and the place where birth occurred and admission to the NICU in U.S. hospitals from January 2016 to December 2016.

Table 9 represents the marital status of the women respondents in the study. A majority of the population who had CLP were married (n=1,230) as compared to the unmarried people who had CLP (n=881).

Table 9

Marital Status and Cleft lip and Palate

Marital status	Cleft lip and palate		Total
	Yes	*No*	
Married	1,230	2,378,194	2,379,424
Unmarried	881	1,568,979	1,569,860
Total	2,111	3,947,173	3,949,284

Table 10 shows the racial distribution of CLP. It is worthy to note that the White population (n=1718) had more CLP babies as compared to Black population (n=219).

Table 10

Mother's Race and cleft lip and Palate

Bridged race of mother	Cleft lip and palate		Total
	Yes	*No*	
White	1,718	2,948,387	2,950,105
Black	219	653,110	653,329
American Indian or Alaskan native	51	434,80	43,531
Asian or Pacific Islander	123	302,196	302,319
Total	2,111	3,947,173	3,949,284

As seen in Table 11, advanced age of the mother did not affect the likelihood of having a baby with CLP. However, 20-24 yrs. (n=501) and 24-29 years (n=599) were the age groups with babies having more CLP. This is because more women fall under this reproductive age group.

Table 11

Mother's Age and Cleft lip and Palate

Mother's age	Cleft lip and palate		Total
	Yes	*No*	
under 15 years	0	2,255	2,255
15-19 years	119	209,775	209,894
20-24 years	501	803,766	804,267
25-29 years	599	1,149,618	1,150,217
30-34 years	545	1,111,732	1,112,277
35-39 years	261	547,751	548,012
40-44 years	76	113,200	113,276
45-49 years	9	8,276	8,285
50-54 years	1	800	801
Total	2111	3,947,173	3,949,284

Table 12 shows the level of education and its association with having a baby with CLP. Level of education and birth outcomes shows an interesting dynamic. While it would be expected that higher education would serve as a protective factor against CLP, the result did not indicate that. Participants with little or no education reported fewer CLP as compared to participants with high school graduate or GED and with some college credit or degree.

Table 12

Mother's Education and Cleft Lip and Palate

Mother's education	Cleft lip and palate		*Total*
	Yes	No	
8th grade or less	82	132,134	132,216
9th through 12th grade with no diploma	284	406,630	406,914
High School graduate or GED Completed	562	979,128	979,690
Some college credit, but not a degree	448	807,416	807,864
Associate degree (AA, AS)	199	322,059	322,258
Bachelor's degree (BA, AB, BS)	342	787,074	787,416
Master's Degree (MA, MS, MEng, Med, MSW, MBA)	143	359,128	359,271
Doctorate (PhD, EdD or professional degree: MD, DDS, DVM, LLB, JD)	28	102,552	102,580
Unknown	23	51,052	51,075
Total	2,111	3,947,173	3,949,284

Table 13 shows the source of payment for delivery. Participants with good income had better pregnancy outcomes as indicated by self-payment as source of payment. This table also shows that those who are on Medicaid (n= 1018) reported to have more babies born with CLP when compared to participants who self-paid for delivery (n=921). This clearly shows that income had an effect on babies born with cleft lip and palate.

Table 13

Mother's Payment Source at Delivery and Cleft Lip and Palate

Payment recode	Cleft lip and palate		Total
	Yes	*No*	
Medicaid	1,018	1,667,102	1,668,120
Private Insurance	921	1,934,565	1,935,486
Self-Pay	86	168,336	168,422
Other	70	153,552	153,622
Unknown	16	23,618	23,634
Total	2,111	3,947,173	3,949,284

Table 14 shows the Body mass index pre- pregnancy. It shows that obesity does to have an impact on the CLP. Respondents with obesity level 1(n=182) and Extreme obesity (n=119) had a low impact on CLP as compared to those who have a normal weight (n=845).

Table 14

Mother's Pre-Pregnancy BMI and Cleft Lip and Palate

Body mass index recode	Cleft lip and palate		Total
	Yes	*No*	
Underweight <18. 5	65	134,666	134,731
Normal 18.5-24. 9	845	1,702,550	1,703,395
Overweight 25.0-29. 9	514	999,717	1,000,231
Obesity I 30.0-34. 9	327	548,475	548,802
Obesity II 35.0-39. 9	182	266,072	266,254
Extreme Obesity III ≥40. 0	119	187,536	187,655
Unknown or not stated	59	108,157	108,216
Total	2,111	3,947,173	3,949,284

Table 15 shows the facility where birth occurred which reveals an interesting dynamic. The anticipated result was that mothers who delivered outside of the hospital should have more babies with CLP due to low-income status. However, this cross tabulation shows that those who delivered in hospital have more CLP (n=2072) as compared to those delivered outside of hospital (n=39). This is because a majority of the participants delivered at the hospital.

Table 15

Facility where Birth Occurred and Cleft Lip and Palate

Facility recode	Cleft lip and palate		Total
	Yes	*No*	
In hospital	2,072	3,883,798	3,885,870
Not in hospital	39	63,173	63,212
Unknown or not stated	0	202	202
Total	2,111	3,947,173	3,949,284

Table 16 shows the birth order and its impact on CLP. The occurrence of CLP is more prevalent in respondents who were having their first, second and third pregnancy as compared to those who have had four or more live births. The incidence decreases as the birth order increases.

Table 16

Total Birth Order and Cleft Lip and Palate

Total birth order	Cleft lip and palate		Total
	Yes	*No*	
1 Live birth	606	1,227,778	1,228,384
2 Live births	562	1,111,374	1,111,936
3 Live births	417	731,664	732,081
4 Live births	220	411,095	411,315
5 Live births	125	213,383	213,508
6 Live Births	75	107,985	108,060
7 Live births	44	55,125	55,169
8 or more live births	53	67,052	67,105

Unknown or not stated	9	21,717	21,726
Total	2,111	3,947,173	3,949,284

Table 17 shows the number of prenatal visits. The expectation was that as the respondents attended more prenatal visits, the incident of CLP would decrease. However, this crosstabulation shows that those who attended no prenatal visits or only 1-2 (n=35) or 3-4 prenatal visits (n=79) have fewer babies born with CLP as compared to those who have 7 to 14 prenatal visits (n=1374).

Table 17

Number of Prenatal Visits and Cleft Lip and palate

Number of prenatal visits	Cleft lip and palate		Total
	Yes	*No*	
No visits	55	61,815	61,870
1 to 2 visits	35	45,766	45,801
3 to 4 visits	79	98,457	98,536
5 to 6 visits	156	192,131	192,287
7 to 8 visits	220	360,300	360,520
9 to 10 visits	429	791,862	792,291
11 to 12 visits	423	993,148	993,571
13 to 14 visits	302	681,923	682,225
15 to 16 visits	189	372,265	372,454
17 to 18 visits	73	103,654	103,727
19 or more visits	103	134,852	134,955
Unknown or not stated	47	111,000	111,047
Total	2,111	3,947,173	3,949,284

Table 18 shows the month when prenatal visit began. The results show that those who started in the 1st to the 3rd month (n=1493) had more babies born with CLP as compared to those who have started their prenatal care from 7th to the final month (n=110) or those who did not have any prenatal care (n=55).

Table 18

Month Prenatal care began and cleft lip and palate

Month Prenatal Care Began	Cleft lip and Palate		Total
	Yes	*No*	
1st to 3rd month	1,493	2,956,237	2,957,730
4th to 6th month	402	640,582	640,984
7th to final month	110	176,741	176,851
No prenatal care	55	61,815	61,870
Unknown or not stated	51	111,798	111,849
Total	2111	3,947,173	3,949,284

Table 19 shows the gestational age at which the CLP babies are born. The results indicate that those who were term, that is 37 weeks or over (n=1744), had more babies with CLP as compared to those who are preterm, that is under 37 weeks (n=365).

Table 19

Gestational age and Cleft lip and palate

Obstetric estimate	Cleft lip and palate		Total
	Yes	*No*	
Under 37 weeks	365	387,004	387,369
37 weeks and over	1,744	3,557,252	3,558,996
3	2	2917	2,919
Total	2,111	3,947,173	3,949,284

Table 20 shows gestational diabetes and babies born with CLP. The results indicated that, those who are with gestational diabetes (n= 162) have fewer babies with CLP as compared to those who did not have gestational diabetes (n=1944).

Table 20

Gestational Diabetes and Cleft lip and palate

Gestational Diabetes	Cleft lip and palate		Total
	Yes	*No*	
No	1,944	3,709,806	3,711,750
Unknown or not stated	5	2,668	2,673
Yes	162	234,699	234,861
Total	2,111	3,947,173	3,949,284

Table 21 shows gestational hypertension and babies born with CLP. The results indicated that, those who are with gestational hypertension (n= 166) have less number of babies with CLP as compared to those who did not have gestational hypertension (n=1940).

Table 21

Gestational Hypertension and cleft lip and palate

Gestational Hypertension	Cleft lip and palate		Total
	Yes	*No*	
No	1940	3,708,985	3,710,925
Unknown or not stated	5	2,668	2,673
Yes	166	235,520	235,686
Total	2,111	3,947,173	3,949,284

Table 22 shows the use of assisted reproductive technology and CLP. The results indicated that use of assisted reproductive technology had an effect on CLP (n= 31) as compared to those who did not use it (n=12).

Table 22

Use of Assisted Reproductive Technology and Cleft lip and palate

Asst. Reproductive Technology	Cleft lip and palate		Total
	Yes	*No*	
No	12	24,238	24,250
Unknown or not stated	6	7,795	7,801
Not Applicable	2062	3,875,689	3,877,751
Yes	31	39,451	39,482
Total	2,111	3,947,173	3,949,284

Table 23 shows the number of babies admitted to Neonatal Intensive Care Unit with CLP. The results show that admission to NICU was less frequent for babies born with CLP (n=691) as compared to those who were not admitted to NICU with CLP (n=1,417).

Table 23

Admission to NICU and Cleft Lip and palate

Admission to NICU	Cleft lip and palate		Total
	Yes	*No*	
No	1,417	3,603,256	3,604,673
Unknown or not stated	3	1,063	1,066
Yes	691	342,854	343,545
Total	2,111	3,947,173	3,949,284

Binomial Logistic Regression Analysis

I used binomial logistic regression as a model to assess how well the independent variables predicted the dependent variable. A logistic regression was performed to ascertain the effects of independent variables on the likelihood that participants had CLP. The variables used in the analysis were cleft lip and palate (dependent variable). The independent variables were advanced maternal age, maternal obesity, number of prenatal visits, month prenatal care began, number of pregnancies, gestational age at birth, assisted reproductive technology used, gestational diabetes, gestational hypertension, marital status, education, and mother's race, payment source for delivery, place where birth occurred, and admission to NICU.

I used binary logistic regression to determine the odds of having a baby with CLP as a pregnancy outcome. To begin, I determined the assumptions of the logistic regression were met so that the result of the analysis would be valid. According to Mertler and Vannatta (2013), the dependent variable needs to be binary or binomial. CLP was categorized as binomial variable, and I coded a baby with CLP as one and a baby without CLP as two. In addition, there should be no multicollinearity. According to Mertler and Vannatta (2013), this can lead to understanding which independent variable contributes to the explained variance. A preliminary multiple linear regression was conducted to evaluate multicollinearity in the variables. As seen in the table, multicollinearity was not violated because tolerance statistics for all the independent variables were greater than 0.1. In addition, the Chi Square test of association shows there was no multicollinearity. There were no outliers and the test of goodness of fit to assess the fit of the model to the data (Mertler & Vannatta, 2013) shows the model is a good fit. This was confirmed by the Hosmer-Lemes which shows that it is statistically significant (p = .000). To start the analysis, I collapsed cells and recoded the variables, but there was no multicollinearity that would negatively impact the analysis, and therefore all the variables were included.

Research Question 1

RQ1: Is there a significant relationship between CLP and maternal reproductive history (advanced maternal age, maternal obesity, number of prenatal visits, month prenatal care began, number of pregnancies, gestational age at birth, assisted reproductive technology used, gestational diabetes, gestational hypertension) among mothers who delivered live infants in U.S. hospitals and birthing centers from January 2016 to December 2016?

$H_0$1: There is no significant relationship with CLP and maternal reproductive history (advanced maternal age, maternal obesity, number of prenatal visits, month prenatal care began, number of pregnancies, gestational age at birth, assisted reproductive technology used, gestational diabetes, gestational hypertension) among mothers who delivered live infants in U.S. hospitals and birthing centers from January 2016 to December 2016.

$H_1$1: There is a significant relationship with CLP and maternal reproductive history (advanced maternal age, maternal obesity, number of prenatal visits, month prenatal care began, number of pregnancies, gestational age at birth, assisted reproductive technology used, gestational diabetes, gestational hypertension) among mothers who delivered live infants in U.S. hospitals and birthing centers from January 2016 to December 2016.

Statistical Analysis for Research Question 1

Table 24 contains Cox and Snell *R* Square and Nagelkerke *R* square values, which are both used to explain variation in the dependent variable. Therefore, the explained variation in the dependent variable based on our model ranges from 0% to 0.5%, depending on whether the reference is Cox & Snell R2 or Nagelkerke R2 methods, respectively. Nagelkerke R square is a modification of Cox & Snell R square, the latter of which cannot achieve a value of one. For this reason, it is preferable to report the Nagelkerke Rsquare value. Based on the outcomes, the amount of variance in the dependent variable accounted for by the model is about 0.5%

Table 24

Model Summary

Step	-2 Log Likelihood	Cox & Snell R Square	Nagelkerke R Square
1	35847.801a	.000	.005

a. Estimation terminated at iteration number 11 because parameter estimates changed by less than .001.

Table 25 shows the classification of the event or category prediction. Binomial logistic regression estimates the probability of an event occurring (in this case, having a baby with CLP). For the event occurring, if the estimated probability is greater than or equal to 0.5 (indicated better than even chance), SPSS statistics will classify the event as occurring (e.g., CLP being present). If probability equals less than 0.5, SPSS Statistics will classify the event as not occurring (e.g., no CLP being present).

Binomial logistic regression is a common method to predict whether cases can be correctly classified (i.e. predicted) from the independent variables. It thus becomes necessary to assess the effectiveness of predicted classifications against actual classification. While many methods are available (which often depend on the nature of the study conducted), all methods revolve around the observed and predicted classifications, which are presented in Table 25.

Table 25 has a subscript, which states, "the cut value is .500." This means that if the probability of a case being classified into the "yes" category was greater than .500, then that particular case is classified into the "yes" category. Otherwise, the case was classified into the "no" category. Table 24 explains that 2,111 cases are classified as having a baby with CLP and 3,947,173 cases are classified as without having baby with CLP, implying that the model correctly classified about 99.9% of the cases.

Table 25

Classification Table

	Predicted		
	Cleft lip and palate		
Step 1 Cleft lip and palate	Yes	No	Percentage correct
Yes	0	2,111	0
No	0	3,947,173	100
Overall Percentage			99.9

a. The cut value is .500

The results presented in Table 26 show that the omnibus goodness-of-fit test for the regression model was statistically significant and reliable in distinguishing or differentiating a baby with or without CLP ($\chi 2$ = 182.158; p = .000).

Table 26

Omnibus Tests of Model Coefficients

		Chi-square	df	Sig.
Step 1	Step	182.158	12	.000
	Block	182.158	12	.000
	Model	182.158	12	.000

The Hosmer & Lemeshow test in Table 27 shows the goodness of fit which suggests the model is a good fit to the data as p=0.725 (>.05). However, the Chi-square statistic on which it is based is very dependent on sample size, so the value cannot be interpreted in isolation from the size of the sample.

Table 27

Hosmer and Lemeshow Test

Step	Chi-square	df	Sig.
1	5.304	8	.725

Table 28 shows regression coefficient (B), the Wald statistic (to test the statistical significance) and the Odds Ratio (Exp (B)) for each variable category. It shows the contribution of each independent variable to the model and its statistical significance. The Wald test ("Wald" column) is used to determine statistical significance for each of the independent variables. An odds ratio is used to measure the relationship that exists between an exposure and an outcome (Szumilas, 2010). This means that given a particular exposure, an outcome will occur compared to the odds that the outcome occurs without the exposure. In other words, odds are “the ratio of probability that an event will occur divided by the possibility that the event will not occur” (Mertler & Vannatta, 2013, p. 298). The regression coefficients are presented in Table 28. The Wald statistics show that mother’s age (p = .000), Maternal Obesity indicated by BMI (p=.020), number of prenatal visits (p = .001), total birth order (p = .001), gestational age at birth ((p = .000), gestational diabetes (p = .002) and gestational hypertension (p = .032) are related to CLP at statistically significant levels (reject the null hypotheses). However, there is no statistical significance among the rest of the variables such as the month prenatal care began (*p* = .369) and assisted reproductive technology (*p* = .369).

The odds Ratio (Exp (B) measure the relationship between exposure and outcome variable. Since the value Exp(β) is less than 1 in some of the variables, this indicates a negative odds or change. Thus, for every increase in variables such as body mass index, total birth order, month prenatal care began, and gestational diabetes during pregnancy, it would lead to the possibility of having a baby with CLP. For example, the odds ratio for age showed that for every increase of 1, there is a 1.080 chance of having a baby with CLP.

From the correlations model in Table 28, mother's age, maternal obesity indicated by BMI, number of prenatal visits, total birth order, gestational age at birth, gestational diabetes and gestational hypertension add significantly to the prediction of whether the mother has a baby with or without CLP (*p* = <.05). The month at which prenatal care began, assisted reproductive technology did not add significantly to the model for prediction of CLP. The odds ratio Exp(B) indicates how the independent variables change the likelihood of the CLP, that is a whether a baby is born with CLP or without CLP. The findings presented in Table 20 reveal high odds for the effects of different maternal characteristic during pregnancy.

The probability of an event occurring can be predicted by using the information in Table 28. It is based on a one-unit change in an independent variable while all other independent variables are kept constant. For example, Table 28 shows that the odds of having CLP ("yes" category) is 4.051 greater with assisted reproductive technology.

Table 28

Variables in Equation

Step 1a	B	S.E.	Wald	Df	Sig.	Exp (B)	Lower	Upper
Mother's Age Recode 9	.077	.020	15.216	1	.000	1.080	1.039	1.122
Body Mass Index Recode	-.031	.014	5.375	1	.020	.969	.944	.995
Number of Prenatal Visits Recode	.034	.010	10.763	1	.001	1.035	1.014	1.056
Month Prenatal Care Began Recode	-.022	.024	.805	1	.369	.978	.933	1.026
Total Birth Order Recode	-.057	.013	18.682	1	.000	.945	.921	.969
Obstetric Estimate Recode	.570	.059	92.345	1	.000	1.768	1.574	1.985
Asst. Reproductive Technology			5.405	3	.144			
Asst. Reproductive Technology (1)	.470	.340	1.909	1	.167	1.600	.821	3.118
Asst. Reproductive Technology (2)	1.399	1.016	1.896	1	.169	4.051	.553	29.68 7
Asst. Reproductive Technology (3)	.377	.184	4.201	1	.040	1.458	1.017	2.091
Gestational Diabetes			12.519	2	.002			
Gestational Diabetes (1)	.254	.083	9.348	1	.002	1.290	1.096	1.518
Gestational Diabetes (2)	-1.744	1.102	2.508	1	.113	.175	.020	1.514
Gestational Hypertension			4.591	1	.032			
Gestational Hypertension (1)	.177	.082	4.591	1	.032	1.193	1.015	1.403
Constant	5.412	.262	428.357	1	.000	224.180		

Interpretation for Question 1

In summary, a binomial logistic regression was performed to ascertain the effects of independent variables of reproductive history to the dependent variable CLP. The logistic regression model was not statistically significant (($\chi 2$ = 182.158; p = .000). The model explained 0.5% (Nagelkerke Rsquare) of the variance in CLP and correctly classified about 99.9% of the cases. The use of reproductive technology is 4.051 times more likely to exhibit in CLP babies than those without CLP. Mother's age (p = .000), maternal obesity indicated by BMI (p=.020), number of prenatal visits (p = .001), total birth order (p = .001), gestational age at birth ((p = .000), gestational diabetes ((p = .002) and gestational hypertension (p = .032) has a statistically significant relationship between CLP and therefore the null hypotheses is rejected. A small p-value (typically ≤ 0.05) indicates strong evidence against the null hypothesis, so we reject the null hypothesis. However, the month at which prenatal care began (p=.369) and assisted reproductive technology (p=.144) shows no statistically significant relationship between CLP, therefore the null hypotheses is accepted.

Research Question 2

RQ2: Is there a significant relationship between socio economic status of the mother (marital status, education, and mother's race, payment source for delivery and place where birth occurred) and CLP resulting in admission to the NICU in U.S. hospitals from January 2016 to December 2016?

$H_0$2: There is no significant relationship between socioeconomic status of the mother (marital status, education, and mother's race, payment source for delivery and place where birth occurred) and CLP resulting in admission to the NICU in U.S. hospitals from January 2016 to December 2016?

$H_1$2: There is a significant relationship between socioeconomic status of the mother (marital status, education, and mother's race, payment source for delivery and place where birth occurred) and CLP resulting in admission to the NICU in U.S. hospitals from January 2016 to December 201

Statistical analysis for Question 2

Table 29 contains Cox and Snell *R* Square and Nagelkerke *R* square values, which are both used to explain variation in the dependent variable. Therefore, the explained variation in the dependent variable based on the model ranges from 0% to 0.29%, depending on whether the reference is Cox & Snell R2 or Nagelkerke R2 methods, respectively. Based on the outcomes, the amount of variance in the dependent variable accounted for by the model is about 0.29%

Table 29

Model Summary

Step	-2 Log likelihood	Cox & Snell R Square	Nagelkerke R Square
1	34971.804[a]	.000	.029

a. Estimation terminated at iteration number 11 because parameter estimates changed by less than .001.

The results presented in Table 30 shows that the omnibus goodness-of-fit test for the regression model and was statistically significant and reliable in distinguishing or differentiating a baby with or without CLP ($\chi 2$ =1058.155; p = .000).

Table 30

Omnibus Tests of Model Coefficients

		Chi-square	df	Sig.
Step 1	Step	1058.155	7	.000
	Block	1058.155	7	.000
	Model	1058.155	7	.000

The Hosmer and Lemeshow test in Table 31 shows the goodness of fit which suggests the model is a good fit to the data as p=.024(<.05). However, the chi-squared statistic on which it is based is very dependent on sample size so the value cannot be interpreted in isolation from the size of the sample.

Table 31

Hosmer and Lemeshow Test

Step 1	Chi-square	df	Sig.
	17.673	8	.024

The regression coefficients are presented in Table 32. The Wald statistics show that mother's education (p = .000), mother's race (p = .000), admission to NICU (p = .000) related to CLP is statistically significant levels. There is no statistical significance among the rest of the variables such as marital status (p=.180), payment source for delivery (p=.057) and facility where baby was delivered (p=.466).

Since the value Exp(β) is less than 1 this indicates a negative odds or change, Thus, for variables, facility where birth occurred and admission to NICU will impact on having a baby with CLP. From the correlations model in Table 24 it shows that mother's education (p = .000), mother's race (p = .000), admission to NICU (p = .000), add significantly to the prediction of whether the mother has a baby with or without CLP (p = <.05). Marital status (p=.180), payment source for delivery (p=.057), facility where baby was delivered (p=.466) did not add significantly to the prediction of CLP. The odds ratio (Exp(B) indicates how the independent variables change the likelihood of the CLP, that is whether a baby with CLP or without CLP.

Table 32

Variables in the Equation

							95% C.I. for EXP(B)	
Step 1a	B	S.E.	Wald	df	Sig.	Exp (B)	Lower	Upper
Marital Status	.116	.049	5.612	1	.018	1.123	1.020	1.236
Mother's Education	.090	.014	43.532	1	.000	1.094	1.065	1.124
Bridged Race Mother	.151	.030	25.066	1	.000	1.163	1.096	1.234
Payment Recode	.042	.026	2.553	1	.110	1.043	.991	1.098
Facility Recode	-.294	.163	3.252	1	.071	.745	.542	1.026
Admission to NICU			1247.552	2	.000			
Admission to NICU (1)	1.641	.047	1241.104	1	.000	5.162	4.712	5.656
Admission to NICU (2)	-.322	.580	.308	1	.579	.725	.233	2.259
Constant	5.678	.208	745.628	1	.000	292.326		

a. Variable(s) entered on step 1: Marital Status, Mother's Education, Bridged Race Mother, Payment Recode, Facility Recode, and Admission to NICU.

Interpretation of Question 2

The results show that marital status of the mother (p = .018) mother's education (p = .000), mother's race (p = .000), admission to NICU (p = .000) has a statistically significant relationship between CLP and therefore the null hypothesis is rejected. The null hypothesis was rejected if p-values were $p \leq 0.05$. However, payment source at delivery and place where birth occurred showed that there is no statistically significant relationship between CLP and these variables. Therefore, the null hypothesis is accepted.

A binomial logistic regression was performed to ascertain the effects of independent variables to the dependent variables. The logistic regression model was not statistically significant ($\chi2$ =1058.155; *p* = .000). The model explained 0.29% (Nagelkerke R2) of the variance in CLP and correctly classified about 99.9% of the cases. Mother's education, mother's race, admission to NICU all had an effect on CLP as in comparison to the other variables. A small p-value (typically ≤ 0.05) indicates strong evidence against the null hypothesis, so we reject the null hypothesis. However, payment source at delivery and facility where birth occurred did not show significance, and therefore the null hypotheses is accepted.

In summary, logistic regression model was used to assess the importance of each independent variable in research question 1 and 2 and to predict which variables had the strongest relationship with each other. Of the predictor variables, Mother's age (*p* = .000), Maternal Obesity indicated by BMI (*p*=.020), number of prenatal visits (*p* = .001), total birth order (*p* = .001), gestational age at birth (*p* = .000), gestational diabetes (*p* = .002) and gestational hypertension (*p* = .032). Mother's education, marital status mother's race, admission to NICU was found to be statistically significant (*p* = <.05). Overall, these variables were statistically significant predictor of relationship between the independent and dependent variables. Therefore, the result shows that there are some maternal characteristics that are related to CLP.

Summary

The purpose of this study was to examine the relationship between CLP and maternal characteristics among women who delivered live births in the United States between January to December 2016. The population studied is diverse and evenly distributed. In this study, I examined if there is a statistically significant relationship between the dependent and the independent variables or the extent to which the independent variables (i.e., advanced maternal age, maternal obesity, number of prenatal visits, month prenatal care began, number of pregnancies, gestational age at birth, assisted reproductive technology used, gestational diabetes, gestational hypertension marital status, education, and mother's race, payment source for delivery and place where birth occurred) predict the dependent variables (i.e., Cleft lip and palate resulting in admission to the NICU in U.S. hospitals from January 2016 to December 2016) based on epidemiological triad theory.

In chapter 4, I reported the data collection procedure, data screening, treatment of missing data, data analysis methods and results. Findings from the study show that there is statistically significant relationship between CLP mother's age, maternal obesity indicated by BMI, number of prenatal visits, total birth order, gestational age at birth, gestational diabetes and gestational hypertension mother's education, marital status mother's race, admission to NICU. The pregnancy outcome showed that there are several variables that were a statistically significant predictor of relationship between the independent and dependent variables and that certain maternal risk factors during pregnancy play a significant role in having a baby with CLP. However, the findings should be interpreted with caution because the participants might have responded in a manner beyond my control. The data did not meet the parametric statistical tests, which limit the extent to which it can be generalized to the larger population, but the findings from the study can be used to develop educational materials and to develop programs and services that will better improve women's pregnancy outcomes. In chapter 5, I discuss the interpretation of the research findings, limitation of the study, recommendations for future research, implications for social change, and conclusion.

Chapter 5: Discussion, Conclusion, and Recommendations

Introduction

The purpose of this quantitative study was to determine if there is a relationship between CLP and maternal characteristics such as reproductive history (advanced maternal age, maternal obesity, number of prenatal visits, month prenatal care began, number of pregnancies, gestational age at birth, assisted reproductive technology used, gestational diabetes, and gestational hypertension), socioeconomic status of the mother (marital status, education, mother's race, payment source for delivery, and place where birth occurred), and admission to the NICU in U.S. hospitals from January 2016 to December 2016. I also assessed the relationship of the independent variables with the birth status of the child with CLP. A binary logistic regression was conducted to assess the relationship between the dependent and independent variables. Results from this analysis showed that some maternal characteristics developed during pregnancy were significantly associated with having a baby born with CLP among U.S. women. In this chapter, I will discuss the results of the study, interpretation of the findings, limitations of the study, and public health implications of the findings. I close the chapter by providing my conclusions and recommendations for further research on CLP.

Interpretation of Findings

My study on maternal characteristics in CLP showed that there are certain maternal characteristics that can serve as predicting factors for CLP. These include mother's age (p = .000), maternal obesity indicated by BMI (p = .020), number of prenatal visits (p = .001), total birth order (p = .001), gestational age at birth (p = .000), gestational diabetes (*p* = .002), and gestational hypertension (*p* = .032). In addition, I found the socioeconomic characteristics of the mother, as indicated by the variables such as mother's education (*p* = .000), marital status of the mother (*p* = .018) mother's race (*p* = .000), and admission to NICU (*p* = .000), to be statistically significant (*p* = <.05) and thus potential predicting factors for CLP.

One result from this study showed that maternal age has a significant relationship (*p* = .000) to CLP. As Myrskylä and Fenelon (2012) explained, birth defects are more often diagnosed in those mothers who have infants when they are below 24 and above 34 years of age. The researchers also concluded that there is a definite link between the age of the mother and adverse offspring outcome (Myrskylä & Fenelon, 2012). Numerous researchers also identified advanced maternal age as a risk factor risk for OFC (Shaw, Croen, & Curry, 1991). Similar to results from other studies, my findings indicated that it is not ideal to deliver at a very young age; rather, it is preferable that adolescent women wait a few years to increase the chances of delivering a healthy baby (Myrskylä & Fenelon, 2012).

Another result from my study indicated that maternal obesity is a contributing factor to CLP. Although in certain studies there are some discrepancies in the results on the maternal biological factors that are related to CLP, researchers have found a strong correlation between risk factors such as diabetes, preexisting diabetes mellitus (DM), hypertension, maternal obesity, and underlying metabolic abnormalities with CLP (Kutbi, 2014). Kutbi (2014) concluded that hypertension may also have an impact on congenital anomalies; however, the literature on these risk factors associated with OFC's is limited

(Kutbi, 2014). Past researchers have also found that mothers who are obese and mothers who are underweight have a higher risk of delivering an infant with OFC (Maneerattanasuporn 2017; Kutbi, 2014). The results of my study further show that there is a significant relationship between obesity and CLP.

There are other contributing factors to CLP such as prenatal care, number of prenatal visits, total birth order, gestational age at birth, gestational diabetes, and gestational hypertension. Literature has shown that prenatal diagnosis is a better means of identifying CLP, and it is always possible to identify craniofacial abnormalities on ultrasounds performed during the prenatal period (Jones, 2002). Therefore, prenatal care and the time at which the prenatal care occurs, as well as the number of prenatal care visits significantly affect the birth outcome. Better counseling can be provided to the women if CLP is detected using ultrasound during pregnancy (Jones, 2002). However, my study indicated that several other aspects of the maternal reproductive history including prenatal care, the birth order, and the gestational age at delivery also had a significant impact on CLP. Therefore, it is important to have coordinated care among health care providers to effectively manage the health of pregnant women and to ensure successful birth outcomes (Iezzoni et al., 2014).

According to Fowler and Jack (2003), prenatal care improves the health-related behavior, services, and social support for women in the United States. Ideally, the initial visit should start during the preconception period, or at least before the first prenatal visit to obtain a baseline assessment of the mother (Mills et al., 1989). The contributing factors to where women obtain prenatal care include their education, occupation, age, parity, family size, and wealth assessments. Researchers have indicated that while the private sector provides more prenatal visits and tests, this does not serve as an indication of an improved birth outcome (Arrieta et al., 2011). Some researchers indicated that the use of ART was related to septal heart defects, and CL with or without CP among single births. Those researchers indicated that some anomalies are found more often in infants who are conceived with ART (Reefhuis et al., 2008). However, my study did not find any significant association between ART and CLP. Similar to findings in Elahi et al.'s (2004) literature review, my findings showed a positive association between increased maternal gravidity and an increased risk of congenital heart defects and isolated CL with or without CP. The researchers indicated that since there is a connection between diabetes, obesity, hypertension, and the increased incidence of OFC's, expectant mothers are encouraged to follow healthy habits, nutritious diet, maintain a healthy weight, and take measures to be screened for probability of diabetes or hypertension before outset and during initial stages of pregnancy (Kutbi, 2014). My study on maternal characteristics and CLP also indicated that gestational diabetes and gestational hypertension have a significant effect on CLP.

Sociodemographic factors can also affect the mother's risk of having an infant with CLP. Specific factors shown to be statistically significant include mother's education, marital status, mother's race, and admission to NICU (Carmichael et al., 2003). These types of OFC's are often associated with a lower maternal education level. In addition, an increase of the risk of OFCs was identified when there was a combination of maternal obesity or underweight (Cedergren & Källén, 2005). Past researchers have also recognized an association between a mother's literacy level and birth outcome (Adanri, 2017; Levine et al., 2004). Researchers also reported that low health literacy affects the women's pregnancy knowledge, which in turn affects the health of the baby (Shieh, Mays, McDaniel &Yu (2009). Rothman et al. (2004) also reported that it was difficult for women with less education to read directions and to follow proper care, which often resulted in worse clinical outcomes. A study conducted in Canada by Auger, Luo, Platt, and Daniel (2008) showed an association between lack of high school diploma level of education and low birth weight. The results from my study showed that higher education would serve as a protective factor against negative birth outcomes. In my study, higher education showed a significant effect on CLP compared to participants with lower education. My finding endorses that there is an association between education level and pregnancy outcome (Kohan, Ghasemi, & Dodangeh, 2007).

In my study of maternal characteristics and CLP, mother's race (p = .000) and admission to NICU (p = .000) were also found to be statistically significant. Researchers have identified that OFCs are associated with a low SES of the mother that include maternal income, educational level and maternal race. Studies of maternal and paternal effects on the incidence of oral clefts among the Caucasian and African American populations in the United States indicated that the prevalence and the rate of oral clefts were higher in children of Caucasian mothers as compared to African American mothers (Thériault, Iturra, & Gingras, 1983). Therefore, low SES, as indicated by marital status, maternal education, race, and income, increases the probability of admission to the NICU, which increases healthcare costs. OFCs are common birth anomalies that may create a considerable burden on the quality and health of the individuals as well as affect the socioeconomic welfare of the affected person and their families (Wehby & Cassell, 2010). According to Wehby and Cassell (2010), there is a substantial increase in healthcare cost and needs that are associated with CLP. The same study also showed that CLP can have a strong impact on outcomes such as the length of stay in the NICU, quality of life, quality of health in the long-term, use of healthcare and its costs, and socioeconomic issues (Wehby & Cassell, 2010).

Researchers have suggested that racial and ethnic differences also have a direct link to many health-related issues and congenital anomalies in infants, some of which are spina bifida, CLP, increased cancer risk, and muscular malformations (Boulet, et al., 2009). Therefore, additional studies have been done to identify the association between racial or ethnic differences and OFCs (Boulet et al., 2009). However, possible lifestyle factors such as maternal tobacco use, proper vitamin supplements, and healthy diet were not assessed by the researchers in the study. Yet, in the context of race, social influences are more likely to play a role than genetic predispositions (DeRoo et al., 2003). Therefore, while it may be useful to know which populations are more susceptible to OFCs, far-reaching and convincing correlations in racial and ethnic differences have not yet been found. For instance, in some areas, the African-American community has less access to health care than Caucasian people, which may result in less than desirable lifestyle factors. Because these social factors are primarily important, increasing pregnancy planning and counseling efforts in high-risk populations may be an effective means of mitigating CLP risk (Charugundala, 2013).

In my study, I did not find a statistically significant predictive relationship between some reproductive factors and some socioeconomic factors. Factors such as the month at which prenatal care began, the payment source at delivery, the facility where the birth occurred, and assisted reproductive technology did not show significance and therefore did not add significantly to CLP in the study population.

The results of my study were in accord with the epidemiological triad theory. The triad, agent, environment, and host played a significant role in the CLP. Causative agent such as maternal reproductive factors can affect the mother to have an unhealthy baby. The socio-cultural factors associated with low prenatal care utilization can be viewed as modifying factors and perceived barriers to health seeking behavior for the women in the study. Furthermore, results from this study indicated the need for prevention-focused programs that specifically target and encourage women to seek medical care as soon as they discover they are pregnant. This may help to promote healthy practices among these women.

In summary, I used the logistic regression model to assess the importance of each independent variable in Research Questions 1 and 2 and to predict which variables had the strongest relationship with each other. Of the predictor variables, many of reproductive characteristics such as mother's age, maternal obesity indicated by BMI, number of prenatal visits, total birth order, gestational age at birth, gestational diabetes, and gestational hypertension were all proven to be significant predictors of CLP. Factors that indicate the sociodemographic status of the population (e.g., mother's education, marital status of the mother, mother's race, and admission to NICU) were also found to be statistically significant ($p = < .05$). Overall, these variables were statistically significant predictors, revealing a significant relationship between maternal characteristics and CLP.

Limitations of the Study

There were several limitations associated with the use of secondary data including limitations based on the sampling schemes. Responses were wholly based on self-reporting which may not always be accurate. There may be difficulties in appropriateness, authenticity, future recall, and memory loss with respect to participant responses. Additional limitations in the form of response bias can also occur in any study reliant on information provided by the participants during data collection (Creswell, 2009). Potential limitations associated with this study included the use of self-reported data, which can introduce recall bias (Creswell, 2007). The probability for future recall bias could occur due to individual responses to the NCHS birth certificate form techniques, questionnaire designs in the form and the mental competency of respondents to recall the entire information provided during the form completion. Such information could not be recollected to completeness. The impact of recall bias can lead to either overestimation or underestimation of the outcomes of this study. Finally, a critical evaluation of the data was conducted to assure that the variables used were consistent with my research topic. In this study, I used secondary, birth certificate data because it was easy to retrieve the publicly available data from CDC WONDER. Although this method may reduce nonresponse bias, it did provide anonymity and participants might not have truthfully answered questions due to problems of recall (Creswell, 2007).

There are certain other limitations in using secondary data and the data assumptions in retrospective data. Validity threat can be affected due to the impact of working with a large proportion of missing data in the file and the researcher cannot control this. However, in my study, a very small amount of missing data was not included for analysis, and therefore it did not have much effect on the results. Statistical analysis and the results obtained can be highly impacted by the presence of missing values. In response, I deleted the cases which had missing values in the data set and dropped off cases of participants who did not complete the birth certificate data. Although not all bias in the study could be controlled, the awareness of the presence of bias allowed thorough scrutiny of the results (Sica, 2006).

Moreover, most of the responses to the pregnancy history and the prenatal care questions in the data were self-reported and self-recalled; thus, one can only assume that patients truthfully recalled their pregnancy history and reported accurate information while answering the questions to complete the birth certificate. In addition, since the inclusion criteria for the study encompassed women under age 18, they may have different feedbacks to the questions in the birth certificate questions due to their lack of experience with antenatal care which could have provided robust data. As reported by Block (2002), there are intrinsic limitations with the self-reporting research method and analysis that relies on empirical measures alone; this is because cognitive and situational factors could affect the validity of the self-administered questionnaires. Cross-referencing with other related variables is a technique to determine the reliability and validity of the self-reported problems; there can be problems due to the misinterpretation of the questions in self-reported data, and this can be a threat to the validity of information (Creswell, 2014). According to Frankfort-Nachmias and Nachmias, (2008), the anonymous and voluntary nature of participation in research study intrinsically increases the likelihood of honest responses provided by participants. My research study will assume that honesty had prevailed to reveal an objective reality. External validity can be described as the extent to which the study findings can be generalized to target population (Crosby, DiClemente, & Salazar, 2006).

Furthermore, the study was limited to women who delivered only live births within the United States, so any women who delivered stillbirths or who had abortions as well as those who delivered outside the U.S. were not included in the study. According to Gliem and Gliem (2003), the use of single item questions in a construct is not a reliable way to generate a conclusion. Since the dependent variable in this study was a single item construct, this could constitute a limitation to the study and present an opportunity for future studies and the development of stronger instruments to support future study.

Recommendations

I conducted this study to augment to the body of literature for CLP research, specifically in the perspective of the potential role of maternal characteristics. My survey of past literature revealed that information and research regarding the role of maternal characteristics in CLP was scant. I therefore decided to conduct this study in order to begin finding any predictable relationships between the aspects of maternal reproductive history, socioeconomic status, and CLP. These observations through the epidemiological triad theory of interaction between the agent, host, and the environment could help provide information to women participants in the study learned through their antenatal visit. This information, along with timely exposure to prenatal care, could help women make better informed decisions about their health during pregnancy and potentially result in fewer births with defects such as CLP.

Out of the nine variables studied in maternal reproductive history, there were seven variables (mother's age, maternal obesity indicated by BMI, number of prenatal visits, total birth order, gestational age at birth, gestational diabetes and gestational hypertension) that had a statistically significant relationship between CLP which could indirectly influence a baby to be affected with CLP. Therefore, it is important for health professionals to disclose the ill effects of birth outcomes to mothers during prenatal visits regarding the age at which they can conceive to have a healthy baby. Educated mothers can significantly impact the healthy outcome of their babies, so educational awareness on prenatal care and other related issues for adolescents in schools and colleges is highly recommended.

Regarding the reproductive history, the women in this study were aware of the importance of antenatal visits. Ninety percent of women attended six or more antenatal visits; more than the four visits or more as proposed by WHO (2002). Although there were more than nine visits for more than eighty percent of the respondents, only seventy percent of these women started antenatal care before the end of the first trimester (three months). It is important to encourage early start of antenatal visits. This will allow early detection of potential medical problems in mothers and will reduce pregnancy complications that can lead to birth defects such as CLP. Less than 10% waited until the last month or had no prenatal visits during their pregnancy. One should note that there was no way to identify the reasons for not attending prenatal visits. Future studies should consider what influences women to wait longer to start antenatal care and how media campaigns could work to remedy this. Therefore, future studies should focus more on parental care delivered to pregnant women. The women recalled all the responses after their delivery and completed the birth certificate data, but if it was collected during pregnancy, the study may give better insight. In addition, future studies should aim at correcting theses important aspects of getting relevant and real-time data.

Out of the seven variables studied in relation to the socioeconomic status of the mother, three variables (mother's education, marital status, mother's race, and admission to NICU) had a statistically significant relationship between CLP. A mother's race, marital status, education, and admission to NICU, which are considered as marks of a mother's sociodemographic factors, can indirectly influence an infant's risk of CLP. Therefore, it is important for health professionals to include these risks for birth outcomes to mothers during prenatal visits.

Health practitioners should be proactive in educating pregnant women during each visit on the importance of self-care and the early start of antenatal care. A mixed methods approach of qualitative and quantitative research would be able to gather more information than this quantitative study, and thus would help to highlight other reasons for lack of attendance or late attendance of antenatal care and what can be implemented to encourage women to use health facilities before, during, and after pregnancy.

Implications

Reducing birth defects is an important goal for public health professionals across the globe. The results from this study showed an interplay between different maternal characteristics and the challenges health professionals encounter in countries such as the United States and elsewhere among the world. These results may help health professionals in reducing risk of birth defects and promoting better pregnancy outcomes. Data from my research study shows that although women in the U.S. are found to have a high level of education, prenatal education should still be introduced in high school and students should be encouraged to take health-related courses emphasizing this subject area, even if they are not majoring in health sciences. Community health promotion and awareness should emphasize early antenatal care to safeguard the health of the mother and child. Although this was not an area of focus in this study, the information that women receive during their routine antenatal visits should address the importance of healthy living for a successful pregnancy outcome. This combination of practices is essential for successful pregnancy outcomes and preventive health education could be useful for behavioral change.

However, no known study to date has been able to address the risk of CLP in relation to a mother's obesity, gestational diabetes, and gestational hypertension. The number of prenatal visits, total birth order, gestational age at birth are contributing factors to the birth defects such as CLP. Thus, education on reducing prevalence of these factors could help reduce the risk of these birth defects. Strong relations developed between community outreach organizations such as colleges and churches and individual healthcare providers to offer comprehensive education on prenatal care, dietary changes, exercise, prevention of maternal diabetes, and hypertension during pregnancy are the best approaches to reduce the incidence of CLP among infants born to American women. Positively impacting socioeconomic factors such as the mother's education also play a huge role in reducing this defect.

Potential positive social change in the communities on healthy behavior could be a good starting point. However, a better starting point may be to realize and understand the complexity of the issues and its consequences. With this understanding in mind, future endeavors could perhaps bring a broader perspective, as well as better information and true openness to effective solutions to better dissect the etiology of CLP. Adapting health programs suitable to the cultural needs and values of a community may be more appropriate than creating preventive health programs that are not accessible to those who actually need them. It is imperative therefore, that future investigations include immigrants, citizens with children born outside the United States and their second .generations in order to implement healthy programs that benefit not only U.S population, but the entire population that are vulnerable to the birth defects.

Conclusions

These study results could provide essential insight into identifying the relationship between risk factors; measures need to be taken to rectify these issues prenatally since children with this defect demand significant medical care and incur significant costs (Alkire, Hughes, Nash, Vincent, & Meara, 2011). With the increase in population, the overall infant morbidity and mortality has decreased over the years. A recent research study is necessary to determine some of the predisposing factors that are contributing to the outcome of these birth defects among women in the United States. Consequently, this research could lead to social change among women by enabling them to understand and avoid certain prenatal behaviors and in result, engage in early and improved care during pregnancy to develop a healthy baby. Results from this research could help healthcare professionals identify risk factors at an earlier stage during prenatal care so further adverse effects could be prevented. Additionally, this study could help reduce the cost of treatment for the children who are affected with cleft lip or cleft palate (Alkire et al., 2011). Furthermore, CLP has an extensive effect on the economic well-being of developing countries; those affected may not have sufficient or any insurance to pay for their treatment, thus preventing those with CLP from accessing the best care (Alkire et al., 2011).

The study's findings also provided enough guidance on interpreting its results and the strategies for prevention, as well as identifying future research activities. It will also enable researchers to understand the significance of the problem amongst women across the United States. These findings will enable the development of specific prevention programs that target women and families who are at high risk for developing CLP, as well as help develop prevention strategies leveraged by the clinician during prenatal care.

Finally, these findings will help thousands of children and their families suffering from CLP to have an improved quality of life. The objective of this study was to identify the primary etiological factors according to past literature, as well as to determine risk factors and understand the problems associated with them. However, to commence a thorough understanding, a thorough review of literature on the topic of CLP is required.

Results of the study may be used to promote positive social change by identifying and assessing challenges in implementing intervention programs meant to assist in controlling CLP among United States populations who are disproportionately affected by this condition. My research results and findings were based on analysis of data from the NCHS national database, and results indicated that prevalence of CLP was significantly higher among the white population that was studied. Of the sixteen predictor variables, problems developed during pregnancy were statistically significant. An increase in problems developed during pregnancy most likely would increase the chance of having negative pregnancy outcomes. It has been established in past literature that having antenatal care and care throughout the pregnancy increases the chance of having a successful pregnancy and healthy child. The results in my study also further support this opinion. However, there is still much to be done to encourage early antenatal care.

Findings from this study could help encourage and guide education in early antenatal care. Aspirations for the long-term effects of this study would be to influence and redesign the educational efforts and healthcare outreach to women who normally would not pursue antenatal health on their own. Healthcare practitioners and providers, state and federal health agencies, and the local community health centers should retool the traditional focus of reaching out and screening women for any illness during pregnancy. Practitioners should also strive to change current statuses of antenatal care. The practice of registering late for antenatal care and having to go for biweekly visits due to a late start needs to be discouraged. Uniformity of care for pregnant women in both private and public health facilities needs to be encouraged to allow women who use government hospitals to have confidence in the care they are receiving.

The healthcare costs incurred from CLP and other associated birth defects can be quite costly for those affected families, costly enough to negatively affect their quality of life—but my findings suggest that there are opportunities to decrease these risks, and therefore the costs, through preventative actions such as better prenatal and antenatal care and education. If one implements observations from this study into both prenatal and antenatal care and prevention, then the risk of CLP and potentially other birth defects and OFC's in infants may be prevented and dramatically reduced among those who are most vulnerable, thus promoting better quality of life not only for future children, but also their families.

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Appendix A: U.S. Standard Certificate of Live Birth

MOTHER

29a. DATE OF FIRST PRENATAL CARE VISIT
____/____/____ (MM DD YYYY) ☐ No Prenatal Care

29b. DATE OF LAST PRENATAL CARE VISIT
____/____/____ (MM DD YYYY)

30. TOTAL NUMBER OF PRENATAL VISITS FOR THIS PREGNANCY
________ (If none, enter ⁄0".)

31. MOTHER'S HEIGHT ____ (feet/inches)

32. MOTHER'S PREPREGNANCY WEIGHT ____ (pounds)

33. MOTHER'S WEIGHT AT DELIVERY ____ (pounds)

34. DID MOTHER GET WIC FOOD FOR HERSELF DURING THIS PREGNANCY? ☐ Yes ☐ No

35. NUMBER OF PREVIOUS LIVE BIRTHS (Do not include this child)
- 35a. Now Living — Number ____ ☐ None
- 35b. Now Dead — Number ____ ☐ None

36. NUMBER OF OTHER PREGNANCY OUTCOMES (spontaneous or induced losses or ectopic pregnancies)
- 36a. Other Outcomes — Number ____ ☐ None

37. CIGARETTE SMOKING BEFORE AND DURING PREGNANCY
For each time period, enter either the number of cigarettes or the number of packs of cigarettes smoked. IF NONE, ENTER ⁄0".

Average number of cigarettes or packs of cigarettes smoked per day.

	# of cigarettes		# of packs
Three Months Before Pregnancy	____	OR	____
First Three Months of Pregnancy	____	OR	____
Second Three Months of Pregnancy	____	OR	____
Third Trimester of Pregnancy	____	OR	____

38. PRINCIPAL SOURCE OF PAYMENT FOR THIS DELIVERY
- ☐ Private Insurance
- ☐ Medicaid
- ☐ Self-pay
- ☐ Other (Specify) ____

35c. DATE OF LAST LIVE BIRTH ____/____ (MM YYYY)

36b. DATE OF LAST OTHER PREGNANCY OUTCOME ____/____ (MM YYYY)

39. DATE LAST NORMAL MENSES BEGAN ____/____/____ (MM DD YYYY)

40. MOTHER'S MEDICAL RECORD NUMBER

MEDICAL AND HEALTH INFORMATION

41. RISK FACTORS IN THIS PREGNANCY (Check all that apply)

Diabetes
- ☐ Prepregnancy (Diagnosis prior to this pregnancy)
- ☐ Gestational (Diagnosis in this pregnancy)

Hypertension
- ☐ Prepregnancy (Chronic)
- ☐ Gestational (PIH, preeclampsia)
- ☐ Eclampsia

- ☐ Previous preterm birth
- ☐ Other previous poor pregnancy outcome (Includes perinatal death, small-for-gestational age/intrauterine growth restricted birth)
- ☐ Pregnancy resulted from infertility treatment-If yes, check all that apply:
  - ☐ Fertility-enhancing drugs, Artificial insemination or Intrauterine insemination
  - ☐ Assisted reproductive technology (e.g., in vitro fertilization (IVF), gamete intrafallopian transfer (GIFT))
- ☐ Mother had a previous cesarean delivery If yes, how many ____
- ☐ None of the above

42. INFECTIONS PRESENT AND/OR TREATED DURING THIS PREGNANCY (Check all that apply)
- ☐ Gonorrhea
- ☐ Syphilis
- ☐ Chlamydia
- ☐ Hepatitis B
- ☐ Hepatitis C
- ☐ None of the above

43. OBSTETRIC PROCEDURES (Check all that apply)
- ☐ Cervical cerclage
- ☐ Tocolysis

External cephalic version:
- ☐ Successful
- ☐ Failed

- ☐ None of the above

44. ONSET OF LABOR (Check all that apply)
- ☐ Premature Rupture of the Membranes (prolonged, ∃12 hrs.)
- ☐ Precipitous Labor (<3 hrs.)
- ☐ Prolonged Labor (∃ 20 hrs.)
- ☐ None of the above

45. CHARACTERISTICS OF LABOR AND DELIVERY (Check all that apply)
- ☐ Induction of labor
- ☐ Augmentation of labor
- ☐ Non-vertex presentation
- ☐ Steroids (glucocorticoids) for fetal lung maturation received by the mother prior to delivery
- ☐ Antibiotics received by the mother during labor
- ☐ Clinical chorioamnionitis diagnosed during labor or maternal temperature ≥38°C (100.4°F)
- ☐ Moderate/heavy meconium staining of the amniotic fluid
- ☐ Fetal intolerance of labor such that one or more of the following actions was taken: in-utero resuscitative measures, further fetal assessment, or operative delivery
- ☐ Epidural or spinal anesthesia during labor
- ☐ None of the above

46. METHOD OF DELIVERY

A. Was delivery with forceps attempted but unsuccessful?
☐ Yes ☐ No

B. Was delivery with vacuum extraction attempted but unsuccessful?
☐ Yes ☐ No

C. Fetal presentation at birth
- ☐ Cephalic
- ☐ Breech
- ☐ Other

D. Final route and method of delivery (Check one)
- ☐ Vaginal/Spontaneous
- ☐ Vaginal/Forceps
- ☐ Vaginal/Vacuum
- ☐ Cesarean
  If cesarean, was a trial of labor attempted?
  - ☐ Yes
  - ☐ No

47. MATERNAL MORBIDITY (Check all that apply) (Complications associated with labor and delivery)
- ☐ Maternal transfusion
- ☐ Third or fourth degree perineal laceration
- ☐ Ruptured uterus
- ☐ Unplanned hysterectomy
- ☐ Admission to intensive care unit
- ☐ Unplanned operating room procedure following delivery
- ☐ None of the above

NEWBORN

NEWBORN INFORMATION

48. NEWBORN MEDICAL RECORD NUMBER

49. BIRTHWEIGHT (grams preferred, specify unit)
____ 9 grams 9 lb/oz

50. OBSTETRIC ESTIMATE OF GESTATION:
____ (completed weeks)

51. APGAR SCORE:
Score at 5 minutes: ____
If 5 minute score is less than 6,
Score at 10 minutes: ____

52. PLURALITY - Single, Twin, Triplet, etc.
(Specify) ____

53. IF NOT SINGLE BIRTH - Born First, Second, Third, etc. (Specify) ____

54. ABNORMAL CONDITIONS OF THE NEWBORN (Check all that apply)
- ☐ Assisted ventilation required immediately following delivery
- ☐ Assisted ventilation required for more than six hours
- ☐ NICU admission
- ☐ Newborn given surfactant replacement therapy
- ☐ Antibiotics received by the newborn for suspected neonatal sepsis
- ☐ Seizure or serious neurologic dysfunction
- ☐ Significant birth injury (skeletal fracture(s), peripheral nerve injury, and/or soft tissue/solid organ hemorrhage which requires intervention)
- 9 None of the above

55. CONGENITAL ANOMALIES OF THE NEWBORN (Check all that apply)
- ☐ Anencephaly
- ☐ Meningomyelocele/Spina bifida
- ☐ Cyanotic congenital heart disease
- ☐ Congenital diaphragmatic hernia
- ☐ Omphalocele
- ☐ Gastroschisis
- ☐ Limb reduction defect (excluding congenital amputation and dwarfing syndromes)
- ☐ Cleft Lip with or without Cleft Palate
- ☐ Cleft Palate alone
- ☐ Down Syndrome
  - ☐ Karyotype confirmed
  - ☐ Karyotype pending
- ☐ Suspected chromosomal disorder
  - ☐ Karyotype confirmed
  - ☐ Karyotype pending
- ☐ Hypospadias
- ☐ None of the anomalies listed above

56. WAS INFANT TRANSFERRED WITHIN 24 HOURS OF DELIVERY? 9 Yes 9 No
IF YES, NAME OF FACILITY INFANT TRANSFERRED TO: ____

57. IS INFANT LIVING AT TIME OF REPORT? ☐ Yes ☐ No ☐ Infant transferred, status unknown

58. IS THE INFANT BEING BREASTFED AT DISCHARGE? ☐ Yes ☐ No

Mother's Name ____

Mother's Medical Record No. ____

Figure 1. U.S. Standard Certificate of Live Birth, 2003 Revision

U.S. STANDARD CERTIFICATE OF LIVE BIRTH

LOCAL FILE NO. BIRTH NUMBER:

CHILD

1. CHILD'S NAME (First, Middle, Last, Suffix)
2. TIME OF BIRTH (24 hr)
3. SEX
4. DATE OF BIRTH (Mo/Day/Yr)
5. FACILITY NAME (If not institution, give street and number)
6. CITY, TOWN, OR LOCATION OF BIRTH
7. COUNTY OF BIRTH

MOTHER

8a. MOTHER'S CURRENT LEGAL NAME (First, Middle, Last, Suffix)
8b. DATE OF BIRTH (Mo/Day/Yr)
8c. MOTHER'S NAME PRIOR TO FIRST MARRIAGE (First, Middle, Last, Suffix)
8d. BIRTHPLACE (State, Territory, or Foreign Country)
9a. RESIDENCE OF MOTHER-STATE
9b. COUNTY
9c. CITY, TOWN, OR LOCATION
9d. STREET AND NUMBER
9e. APT. NO.
9f. ZIP CODE
9g. INSIDE CITY LIMITS? □ Yes □ No

FATHER

10a. FATHER'S CURRENT LEGAL NAME (First, Middle, Last, Suffix)
10b. DATE OF BIRTH (Mo/Day/Yr)
10c. BIRTHPLACE (State, Territory, or Foreign Country)

CERTIFIER

11. CERTIFIER'S NAME: ____________________
TITLE: □ MD □ DO □ HOSPITAL ADMIN. □ CNM/CM □ OTHER MIDWIFE
□ OTHER (Specify)____________________
12. DATE CERTIFIED ____/____/______ MM DD YYYY
13. DATE FILED BY REGISTRAR ____/____/______ MM DD YYYY

INFORMATION FOR ADMINISTRATIVE USE

MOTHER

14. MOTHER'S MAILING ADDRESS: 9 Same as residence, or: State: City, Town, or Location:
Street & Number: Apartment No.: Zip Code:
15. MOTHER MARRIED? (At birth, conception, or any time between) □ Yes □ No
IF NO, HAS PATERNITY ACKNOWLEDGEMENT BEEN SIGNED IN THE HOSPITAL? □ Yes □ No
16. SOCIAL SECURITY NUMBER REQUESTED FOR CHILD? □ Yes □ No
17. FACILITY ID. (NPI)
18. MOTHER'S SOCIAL SECURITY NUMBER:
19. FATHER'S SOCIAL SECURITY NUMBER:

INFORMATION FOR MEDICAL AND HEALTH PURPOSES ONLY

MOTHER

20. MOTHER'S EDUCATION (Check the box that best describes the highest degree or level of school completed at the time of delivery)
- □ 8th grade or less
- □ 9th - 12th grade, no diploma
- □ High school graduate or GED completed
- □ Some college credit but no degree
- □ Associate degree (e.g., AA, AS)
- □ Bachelor's degree (e.g., BA, AB, BS)
- □ Master's degree (e.g., MA, MS, MEng, MEd, MSW, MBA)
- □ Doctorate (e.g., PhD, EdD) or Professional degree (e.g., MD, DDS, DVM, LLB, JD)

21. MOTHER OF HISPANIC ORIGIN? (Check the box that best describes whether the mother is Spanish/Hispanic/Latina. Check the "No" box if mother is not Spanish/Hispanic/Latina)
- □ No, not Spanish/Hispanic/Latina
- □ Yes, Mexican, Mexican American, Chicana
- □ Yes, Puerto Rican
- □ Yes, Cuban
- □ Yes, other Spanish/Hispanic/Latina

(Specify)____________________

22. MOTHER'S RACE (Check one or more races to indicate what the mother considers herself to be)
- □ White
- □ Black or African American
- □ American Indian or Alaska Native (Name of the enrolled or principal tribe)__________
- □ Asian Indian
- □ Chinese
- □ Filipino
- □ Japanese
- □ Korean
- □ Vietnamese
- □ Other Asian (Specify)__________
- □ Native Hawaiian
- □ Guamanian or Chamorro
- □ Samoan
- □ Other Pacific Islander (Specify)__________
- □ Other (Specify)__________

FATHER

23. FATHER'S EDUCATION (Check the box that best describes the highest degree or level of school completed at the time of delivery)
- □ 8th grade or less
- □ 9th - 12th grade, no diploma
- □ High school graduate or GED completed
- □ Some college credit but no degree
- □ Associate degree (e.g., AA, AS)
- □ Bachelor's degree (e.g., BA, AB, BS)
- □ Master's degree (e.g., MA, MS, MEng, MEd, MSW, MBA)
- □ Doctorate (e.g., PhD, EdD) or Professional degree (e.g., MD, DDS, DVM, LLB, JD)

24. FATHER OF HISPANIC ORIGIN? (Check the box that best describes whether the father is Spanish/Hispanic/Latino. Check the "No" box if father is not Spanish/Hispanic/Latino)
- □ No, not Spanish/Hispanic/Latino
- □ Yes, Mexican, Mexican American, Chicano
- □ Yes, Puerto Rican
- □ Yes, Cuban
- □ Yes, other Spanish/Hispanic/Latino

(Specify)____________________

25. FATHER'S RACE (Check one or more races to indicate what the father considers himself to be)
- □ White
- □ Black or African American
- □ American Indian or Alaska Native (Name of the enrolled or principal tribe)__________
- □ Asian Indian
- □ Chinese
- □ Filipino
- □ Japanese
- □ Korean
- □ Vietnamese
- □ Other Asian (Specify)__________
- □ Native Hawaiian
- □ Guamanian or Chamorro
- □ Samoan
- □ Other Pacific Islander (Specify)__________
- □ Other (Specify)__________

Mother's Name ______

Mother's Medical Record No. ______

26. PLACE WHERE BIRTH OCCURRED (Check one)
- □ Hospital
- □ Freestanding birthing center
- □ Home Birth: Planned to deliver at home? 9 Yes 9 No
- □ Clinic/Doctor's office
- □ Other (Specify)____________

27. ATTENDANT'S NAME, TITLE, AND NPI
NAME: ____________ NPI:______
TITLE: □ MD □ DO □ CNM/CM □ OTHER MIDWIFE
□ OTHER (Specify)____________

28. MOTHER TRANSFERRED FOR MATERNAL MEDICAL OR FETAL INDICATIONS FOR DELIVERY? □ Yes □ No
IF YES, ENTER NAME OF FACILITY MOTHER TRANSFERRED FROM:
____

REV. 11/2003

Appendix B: Agreement to Use Data

Centers for Disease Control and Prevention
CDC 24/7: Saving Lives, Protecting People™

Data User Agreement

Warning! Data Use Restrictions Read Carefully Before Using

The Public Health Service Act (Section 308 (d)) provides that the data collected by the National Center for Health Statistics (NCHS), Centers for Disease Control and Prevention (CDC), may be used only for the purpose of health statistical reporting and analysis.

Any effort to determine the identity of any reported case is prohibited by this law.

NCHS does all it can to assure that the identity of data subjects cannot be disclosed. All direct identifiers, as well as any characteristics that might lead to identification, are omitted from the dataset. Any intentional identification or disclosure of a person or establishment violates the assurances of confidentiality given to the providers of the information. Therefore, users will:

1. Use the data in this dataset for statistical reporting and analysis only.
2. Make no use of the identity of any person or establishment discovered inadvertently and advise the Director, NCHS, of any such discovery.
3. Not link this dataset with individually identifiable data from other NCHS or non- NCHS datasets.

By using these data you signify your agreement to comply with the above-stated statutorily based requirements.

Related Sites

Data Linkage (http://wwwdev.cdc.gov/nchs/data-linkage/index.htm)

NCHS Data Visualization Gallery (http://www.cdc.gov/nchs/data-visualization/)

Research Data Center (http://wwwdev.cdc.gov/rdc)

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