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Prevalence and predictors of adverse effects of medical care in patients with cleft lip and palate undergoing facial bone repairs and orthognathic surgical procedures in the United States

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PREVALENCE AND PREDICTORS OF ADVERSE EFFECTS OF MEDICAL CARE IN PATIENTS WITH CLEFT LIP AND PALATE UNDERGOING FACIAL BONE REPAIRS AND ORTHOGNATHIC SURGICAL PROCEDURES IN THE UNITED STATES

by

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CERTIFICATE OF APPROVAL

MASTER'S THESIS

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ABSTRACT

BACKGROUND AND SIGNIFICANCE: Almost 15% of newborns have congenital anomalies that involve the oral and craniofacial regions, but of these congenital anomalies, cleft lip and palate and craniosynostosis are the most common. It is estimated that the incidence of cleft lip and palate is 0.664 in 1000 live births. These patients commonly have skeletal imbalances of the maxillae and mandible that require surgical and orthodontic correction. Orthodontists and oral surgeons play a critical role in identifying the necessary care and ensuring that the patient receives the best quality of care possible.

OBJECTIVES: The objective of the current study is to examine the prevalence of adverse effects of medical care and infectious complications in patients with cleft lip/palate undergoing facial bone repairs/orthognathic surgeries in the United States during the years 2012 to 2014. It will also examine the association between patient/hospital related factors and surgical outcomes (including adverse affects of surgery, incidence of infection, etc.) and how these surgical outcomes impact the hospital costs and length of stay in the hospital.

MATERIALS AND METHODS: The Nationwide Inpatient Sample (NIS) is a 20% stratified probability sample of hospitalizations occurring in all acute care hospitals in the United States. It is part of the Healthcare Cost and Utilization Project (HCUP) sponsored by the Agency for Healthcare Research and Quality (AHRQ) [12]. Each hospital in this sample provides information on 20% of hospitalizations occurring during the select years. Hospital stratification is based on multiple hospital-associated variables including: hospital location, geographic region, bed size, teaching status, and ownership/control. Each hospitalization is assigned a sampling weight. Patient-related variables are also provided by the hospitals. In this study, this information is used to provide a nationally representative estimate of all hospitalizations and associated outcomes in the United States from 2012-2014.

RESULTS: This study includes all 1,785 patients with cleft lip/palate undergoing facial bone repair/orthognathic surgical procedures in the United States during the study period (2012-2014). These results confirm the hypothesis that there are a combination of patient and hospital related factors that contribute to the occurrence of adverse events and that the occurrence of these events is associated with substantial increases in hospital charges and length of hospital stay.

CONCLUSION: These study results are a national representative sample of patients with cleft lip/palate undergoing bony facial repair and orthognathic surgery. They reflect the practice patterns and hospitalization outcomes across the United States. These results can serve as a platform for future prospective controlled studies to examine the risk factors associated with adverse effects of medical care for a wide range of surgical procedures. This information is useful for clinicians, health policy makers, and patients so that they can make informed treatment and policy decisions as well as continue to improve surgical procedures and outcomes.

PUBLIC ABSTRACT

Almost 15% of newborns have congenital anomalies that involve the mouth, skull, and facial regions, but the most common of these anomalies is cleft lip/palate and craniosynostosis, a condition where one or multiple sutures of the skull close early and cause problems with normal brain and skull growth. It is estimated that the incidence of cleft lip and palate is 0.664 in 1000 live births. These patients commonly have skeletal imbalances of the upper and lower jaws and face that require surgery and braces. Orthodontists and oral surgeons play a critical role in identifying the necessary care and ensuring that the patient receives the best quality of care possible.

These surgeries typically require inpatient hospital stay for a few days. Patients with cleft lip/palate present with a wide range of syndromes and comorbidities that increase the risk of adverse events or infections. However, while multiple studies have examined complications, to our knowledge there are no nationally representative estimates of the frequently occurring medical errors and infectious complications in patients undergoing facial bone repairs/orthognathic surgeries in hospital settings.

This study uses a national data sample of cleft lip/palate patients undergoing surgery from 2012-2014 to examine the prevalence of negative side affects of surgery, such as infection or other complications. Our results confirm our prediction that there are multiple patient and hospital related factors that can contribute to the occurrence of unwanted surgical events and that these outcomes are associated with substantial increases in hospital charges and length of hospital stay.

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INTRODUCTION

Orthognathic surgery is often necessary for the successful treatment of severe skeletal discrepancies. The American Association of Oral and Maxillofacial Surgery considers Orthognathic surgery medically appropriate in cases with anteroposterior, vertical, and/or transverse skeletal discrepancies that are two or more standard deviations from the published norms as well as anteroposterior, transverse, or lateral asymmetries greater than 3 mm [1,2]. It is also indicated for the treatment of facial skeletal discrepancies, associated temporomandibular joint pathoses, psychological disorders, speech impairment, sleep apnea, airway defects and soft tissue discrepancies [1, 2].

For decades, the majority of patients seeking orthognathic surgery were Class II division I followed by Class III [3-7]. However, in recent years this has reversed despite the fact that Class II division 1 remains the most prevalent pattern. The cause for the reversal is hypothesized to be due to the availability of more non-compliant orthodontic options for the treatment of Class II discrepancies and insurance companies considering surgical treatment more of a necessity for the treatment of Class III [3-7]. The social stigma associated with prominent chins indicating more aggressive behavior and the fact that Class III patterns are more frequently associated with long faces and asymmetries could also make Class III patients more motivated to seek orthognathic correction [6].

Despite the success of surgical treatment in the treatment of severe skeletal discrepancies, patients, parents, and even some orthodontists are often reluctant to proceed with such procedures due to possible complications. Several studies have estimated the prevalence of complications and their impact on outcomes following orthognathic surgeries [8-11]. Common complications of orthognathic surgery include bleeding, swelling, nausea, vomiting, nerve damage, and nose deformities. Studies have reported neurosensory deficit (mild in 32% of patients and disturbing in 3%) as the most common complication. The most serious complication was severe intra operative bleeding [8-11]. The literature reports serious complications to be very rare and there are several studies reporting no fatalities.

While multiple studies have examined complications [8-11], to our knowledge, to date there are no nationally representative estimates of frequently occurring medical errors and infectious complications in patients undergoing facial bone repairs/orthognathic surgeries in hospital settings. The objective of the current study is to examine the prevalence of adverse effects of medical care and infectious complications in patients with cleft lip/palate undergoing facial bone repairs/orthognathic surgeries in the United States during the years 2012 to 2014. We hypothesized that a combination of patient and hospital level factors could contribute to the occurrence of these events and the occurrence of these events is associated with substantial increases in hospital charges and length of stay in the hospital.

LITERATURE REVIEW

Non-Surgical Treatment Options and the Importance of Orthognathic Surgery: Each year tens of thousands of orthognathic surgeries are performed in the United States, amounting to millions of dollars in hospital charges. These complex surgeries are used to treat a variety of patients, including, but not limited to patients with growth imbalances, hyperplastic or hypoplastic jaw relationships, vertical maxillary excess growth, asymmetric growth, craniofacial anomalies, systemic syndromes, and cleft lip with or without cleft palate. Many patients undergoing orthognathic surgery have craniofacial skeletal discrepancies in conjunction with congenital syndromes. Other patients are non-syndromic, but have a growth imbalance between the maxillae and mandible in the vertical, anteroposterior, and/or transverse dimensions that necessitates surgery to improve patient function, esthetics, and psychosocial wellbeing.

Growing patients may be treated via an orthopedic approach to alter, but not normalize their growth patterns. Even with aggressive orthopedic treatment during the patients' growth period, some patients still benefit from orthognathic surgery because orthopedic treatment does not normalize growth patterns nor does it increase the magnitude of the growth a patient will achieve. The success of this approach is dependent on the individual patient's compliance, magnitude of the skeletal discrepancy, and the amount of favorable growth remaining at the time orthopedic treatment is initiated. In order for orthopedics to be successful enough to eliminate the need for surgery, the patient must have a mild to moderate discrepancy and favorable growth remaining.

Oftentimes, non-growing patients with severe skeletal discrepancies cannot be successfully treated orthopedically and are more likely to need surgery [47].

Some patients with mild to moderate growth imbalances may be treated with orthodontics alone, also known as “masking” or “camouflage” treatment. Masking is an orthodontics only intervention and it does not address the underlying skeletal discrepancy, growth imbalance, or jaw relationship. It often appropriately interdigitates the teeth or improves esthetics, but the goal of masking treatment is not to improve the skeletal jaw relationships. As is true for orthopedic treatment, masking is best for mild to moderate cases and is not as successful when attempted in cases with severe skeletal imbalances [47].

Other growth imbalances necessitate a combination of orthopedics and masking treatment. The goal of orthopedic treatment is to alter a patient’s growth to improve their jaw relationship. The amount of favorable growth that remains, the patients’ compliance, and the magnitude of the skeletal discrepancy are all factors that determine whether or not orthopedics will be successful. When treated early and during the patient’s growth spurt, sometimes orthopedic treatment may fully correct the jaw discrepancy. Oftentimes, due to multiple factors, orthopedic treatment alone is not enough to achieve an optimal outcome. In these cases, orthopedic treatment may decrease the magnitude of the skeletal disharmony enough to then successfully treat the patient with orthodontics, ultimately using a masking approach, rather than surgery [47].

However, for many patients, the magnitude of the discrepancy, function, and esthetic needs of the patient warrants surgical intervention and a multidisciplinary approach to treatment. This must be determined on a case-by-case basis after a thorough exam that includes radiographs, photos, and intraoral models. There are many cases in which orthognathic surgery is the best treatment option to improve esthetics, function, speech, and psychosocial well-being. This is often the case for patients with cleft lip/palate [47].

Presurgical Infant Orthopedics: Syndromic and non-syndromic orofacial clefts are among the most common birth defects. The incidence of cleft lip and palate is estimated to be 0.664 out of 1000 live births [25]. Some syndromes associated with cleft lip/palate include Van der Woude Syndrome, Pierre Robin sequence, Velocardiofacial syndrome, and median facial dysplasia. Early recognition of cleft lip/palate, along with any existing associated syndromes is essential for effective orthodontic and surgical intervention.

An entire craniofacial team of doctors and specialists is imperative for the successful growth and development of the patient. This includes feeding specialists, nurses, plastic surgeons, oral surgeons, otolaryngologists, dentists, orthodontists, prosthodontists, geneticists, speech therapists, and sometimes social workers [35]. Due to the severe sequelae of cleft lip/palate, medical intervention begins at a very young age for these children. These patients may suffer from altered facial and oropharyngeal musculature arrangement and function, facial bone structure and growth patterns, velopharyngeal function, speech and sound production, and sinus partitioning and function [35]. Some doctors perform pre-surgical infant orthopedic treatment as early as five weeks old [36]. Pre-surgical infant orthopedic treatment approaches include lip taping, fixed surgical Latham appliance, or nasoalveolar molding. These approaches usually begin around five weeks of age and require many dental visits as well as compliance and help from the parent or guardian. Pre-surgical orthopedic treatments enhance surgical lip repair by reducing tension and provides a skeletal base for the nose [36]. Before infant orthopedics became common practice, eight percent of patients experienced dehiscence. Dehiscence rates have decreased to only three percent now that pre-surgical orthopedics is a more popular treatment option [36]. These techniques approximate the left and right cleft segments to make an easier surgery possible [39, 40]. Impressions for pre-surgical orthopedic appliances may occur as early as two weeks of age. Insertion of these appliances at five weeks of age requires general anesthesia, overnight hospital stay to monitor the airway and feeding, and follow up over the appliance activation period [35]. The appliance is removed five to eight weeks after insertion, at the surgical lip adhesion appointment. Ideally, surgical lip repair occurs one and a half months later. Palatal repair occurs around ages nine to ten months.

Naso-alveolar molding (NAM) is another approach to pre-surgical infant orthopedics. NAM appliances use acrylic plates and nasal stents to mold and reposition the deformed nasal cartilages, columella, and alveolar processes prior to the primary lip repair and nasal surgery. This is done in the neonatal period while the immature cartilage is still malleable and capable of permanent correction [41]. These appliances typically require weekly dental appointments for adjustments. These movements are done slowly, over the course of a few months. Pre-surgical infant orthopedic treatment is still controversial and is not used at all cleft lip and palate centers.

Those who are skeptics of pre-surgical infant orthopedic treatment believe the benefits do not outweigh the burden that this treatment puts on the family. They believe that long-term, presurgical infant orthopedics increases expenses and the burden on the families because these techniques have the potential to inhibit future maxillary growth [35]; this in turn may increase the likelihood that the patient will need orthognathic surgery later in life [42].

Palatal Expansion and Alveolar Bone Grafting: Unilateral as well as bilateral cleft lip and palate introduces asymmetries into the maxillary arch. Prior to alveolar bone grafts, presurgical expansion is often necessary.
Expansion gives the surgeon better access to the bone graft site and improves the maxillary and mandibular jaw relationships. Due to the young age at which these grafts must be performed and the frequency of relapse in the transverse dimension, re-expansion may be necessary.

There are different approaches to timing of alveolar bone grafting. Primary bone grafting occurs in patients under two years told. When an alveolar bone graft is performed in patients between 2-5 years of age, it is known as early secondary bone grafting. Bone grafting after age five is known as secondary bone grafting [38]. Timing of alveolar bone grafting depends largely on viable permanent teeth, specifically the central and lateral incisors adjacent to the alveolar cleft site. If the patient has a viable permanent lateral incisor or if the permanent central incisors approximate the alveolar cleft site, bone grafting is recommended between ages 5-9. This is to provide a bony scaffold and give the permanent teeth the best chance of successful, healthy eruption [35]. However, this is not a hard and fast rule; some craniofacial centers perform alveolar bone grafts later, around the time of eruption of maxillary permanent canines. Alveolar bone grafts serve to stabilize the arch segments to maintain palatal width, improve continuity of the maxillary alveolar ridge, as well as support the alar base [35] and provide enough bone for eruption of permanent teeth, orthodontics, and in some cases, implants to replace missing or lost teeth. In cases of bilateral cleft lip and palate, the bone graft is used to stabilize the premaxilla [35].

Pre-surgical orthopedics, slow palatal expansion, cleft lip and palate repair, alveolar bone grafting, and phase I orthodontic treatment all set the stage for orthognathic surgery later in life. The orthognathic surgery phase of treatment is usually performed when the patient is a teenager, once midface and mandibular growth is complete and the patient has his or her permanent dentition [35].

Growth Patterns in Patients with Cleft Lip/Palate: Patients with unrepaired cleft lip/palate generally have favorable jaw growth.Patients with unrepaired cleft lip/palate more commonly have a posterior crossbite than patients without a cleft, but there are no significant differences in vertical or anteroposterior skeletal jaw relationships in patients with untreated clefts and those without cleft lip/palate [47]. Multiple studies have reported that individuals with untreated cleft lip/palate have normal growth patterns and harmony between the maxilla and the mandible compared to patients who received cleft lip/palate repair during early childhood. This implies that early surgical intervention during jaw development may alter the growth potential of the maxilla, resulting in maxillary and mandibular skeletal discrepancies [43]. On the other hand, there are significant disturbances in maxillary growth in patients who undergo surgical repairs of the cleft site [43]. It is thought that, while necessary, early repair of cleft lip/palate causes scar tissue build up. This scar tissue is thought to alter skeletal jaw growth and restrict normal midface growth [43].

Maxillary hypoplasia in all three dimensions (vertical, transverse, and sagittal) is the most common skeletal disharmony in teenage children with cleft lip/plate who have undergone lip/palate revision surgeries [35]. A hypoplastic maxilla affects the alveolus, dentition, and adjacent soft tissue as well [43].

This maxillary hypoplasia usually manifests as a Class III skeletal and dental relationship. Despite the correlation between early palatal and lip repair surgeries and a Class III malocclusion, these surgeries are necessary to help young children function, feed, and learn to speak. Therefore, most surgeons elect to perform early surgeries and then undergo orthognathic surgery as needed when the patient completes his or her growth.

Cleft lip/palate patients undergo multiple surgeries very early in life. Each of these surgeries has the potential to impact skeletal growth. Cleft lip repair is usually performed before the patient is 3 months old and can affect the morphology of the anterior maxilla. This may be related to the discontinuity defect of the alveolar cleft. Bone grafting of the alveolar cleft defect in early childhood can severely inhibit maxillary growth, which is why some authors believe that bone grafting should be delayed until just prior to eruption of the permanent maxillary canine, between ages 9-12. The hope with this approach is to allow more maxillary growth before surgical intervention [43].

Among these patients, complete unilateral clefts present with the most complicated growth patterns. Some common findings in patients with a cleft lip/palate include an underdeveloped maxilla, which causes nasal bone deflection, intrusion into the pharyngeal space, and a more posteriorly positioned soft palate. As these patients continue to grow, the maxilla remains hypoplastic, while the mandible follows a normal growth pattern. This results in a Class III skeletal pattern with a retrusive maxilla, hypoplastic midface, and relatively prognathic mandible [43].

Presurgical Orthodontics and Orthognathic Surgery: Presurgical orthodontic treatment is almost always needed prior to surgical correction of the skeletal jaw relationship. The goal of presurgical orthodontics is to align and level the teeth over the basal bone in the upper and lower jaws while correcting crowding, rotations, malpositioned teeth, and crossbites. Consideration must be made to address periodontal disease, oral hygiene, and caries prior to surgery. These cases often present with the additional challenge of missing, supernumerary, or malformed teeth as well as teeth with a hopeless prognosis due to their approximation to the cleft site or lack of bone around the root apices. Maxillary lateral incisor teeth are commonly missing in patients with a cleft. Consideration must be made for each of these cases to determine if the natural canine can be protracted into the site of the lateral incisor or if an implant or prosthetic option is needed [43].

The most common orthognathic surgical procedure used to treat these cases is a LeFort I osteotomy, or in more severe class III cases (7-10mm discrepancies), a two jaw surgery is indicated. After growth cessation, if a two jaw surgery is indicated, a LeFort I maxillary advancement combined with a bilateral sagittal split osteotomy (BSSO) setback is commonly used to improve the jaw relationship [35].

In an extremely hypoplastic maxilla with a large skeletal discrepancy, a maxillary distraction procedure may be indicated. Data collected from a single surgeon from 2000-2007 includes 4 male and 4 female cleft lip and palate patients. These patients underwent a Lefort osteotomy with pterygomaxillary disjunction. Two patients underwent external distraction and six patients had internal distraction. The range of maxillary advancement was between 7-19mm, with an average advancement of 12.6mm. Seven of the eight patients (87.50%) experienced difficulties or complications, with the most common complication being associated with device failure; three patients experienced device failure. The complications of all seven patients include: one with intraoperative hemorrhage, one with tooth avulsion, three with device failure, two with significant pain during device activation, one with dissociation of dental anchorage of an external system, two with labial ulcerations, and one with maxillary sinusitis. This study concludes that complications for cleft lip and palate patients are common in distraction cases; however most difficulties are related to the materials or distractors themselves rather than to the osteotomy, and therefore, if handled appropriately, do not typically alter the final result of the surgery [31].

Surgical intervention, along with orthodontics and routine dental care is essential for successful growth and development, function, and esthetics of patients with cleft lip/palate. Existing research confirms that improvement in craniofacial anomalies and an improvement in dentofacial esthetics via multidisciplinary surgical and orthodontic treatment does have a positive impact on patients' psychosocial wellbeing and quality of life. 93% of patients reported a moderate to large improvement in facial appearance, while 64% reported improved chewing function. 60% of patients found that they were more comfortable after surgery and 32% of orthognathic surgery patients found improvements in speech [32].

Despite these and other benefits, there has been a decrease in the number of orthognathic surgeries performed within the last twenty years. The reason for this decrease is likely multifactorial.

Decreases in Orthognathic Surgery – Length of Hospital Stay and Surgical Costs: One contributing factor is likely the corresponding decrease in reimbursement by medical insurance providers. Of the patients who elected to have orthognathic surgery, Medicaid and Medicare insurance were the primary payers in only 9.1% and 4.3% of these cases, respectively [14, 24, 25]. In a national survey published by the Plastic Reconstructive Surgery Journal, both oral surgeons and plastic surgeons noted a decrease in orthognathic surgical procedures in recent years. Of those who noted a decrease, 77.3% of plastic or oral surgeons believe the decrease was attributable to insurance coverage. Within the same time frame, there has been an increase in the number of patients with craniofacial anomalies, including cleft lip/palate. For such patients, multidisciplinary care is essential for the health and longevity of the oral cavity [34].

In most cases, orthognathic surgery requires admission to the hospital and an overnight stay. Depending on the type of procedure performed, the patient's overall pre-surgical health and systemic condition, perioperative events, and individualized patient recovery, patients may require an extended length of stay in the hospital. Surgical and hospital costs have increased in the last decade. In 2008, the mean hospital charges for orthognathic surgery in the United States was $47,348. This amounted to $466.8 million dollars in hospital bills during that year [14]. Surgical intervention and orthodontic treatment is significantly more expensive for patients with cleft lip/palate than patients without these craniofacial anomalies. In 2012-2013, the mean hospital charge for patients with craniofacial anomalies was $139,317, compared to $56,189 for patients without craniofacial anomalies [34]. This may be attributed to the additional procedures, equipment, appointments, and longer hospital stay that cleft lip/palate patients require. These more complex procedures typically require surgeons and orthodontist who have additional fellowship training and expertise, which increases the treatment costs.

Despite the importance of orthognathic surgery for patient esthetics, function, and self-esteem, patients and their families may be hesitant to undergo orthognathic surgery due to fear of the surgical procedure, costs, decrease in insurance coverage, and the complications associated with surgery. The high costs associated with surgery and the lack of reimbursement rates by insurances may be one reason patients are choosing a "masking" or orthodontics only option, even if they can benefit functionally and esthetically from a surgical approach to treatment [14]. In some cases, orthognathic surgery is the only option to accomplish these esthetic and functional treatment goals and provide patients with a healthy, stable occlusion. However, the increasing costs of surgery and decreasing reimbursement by insurance may be causing a decrease in the number of orthognathic surgeries performed each year. There is a concern that orthognathic surgery could become a cosmetic procedure and only available to those who can afford it, rather than to all patients in need. Multiple studies have shown the importance of orthognathic surgery to a patient's overall wellbeing. This suggests that improvement in facial anomalies and improved esthetics has a positive influence on psychosocial status and overall improvement in patients' quality of life [28]. Thus, continued studies of orthognathic surgical treatments and outcomes are an important part of improving these treatments and providing patients with much needed care.

Retrospective Studies of Patients with Craniofacial Anomalies: There are a few retrospective studies analyzing hospital charges, length of hospital stay, and surgical outcomes in patients with congenital craniofacial anomalies; however, none of these articles specifically study patients with cleft lip/palate undergoing orthognathic surgery.

One retrospective study analyzed Nationwide Inpatient Sample data between the years 2004-2010. Over this 6 year period, the dataset includes 8,340 patients who underwent orthognathic surgery, all of whom had cleft lip, cleft palate, or another craniofacial anomaly. These patients are identified via the ICD-9-CM diagnosis codes and these patients have a range of syndromes or anomalies including: cleft lip with or without cleft palate, acromegaly, congenital musculoskeletal deformities of the face, jaw, or skull (facial asymmetries, compression facies, depressions in the skull, deviated nasal septum, congenital dolichocephaly, plagiocephaly, Potter's facies, congenital squashed nose), Apert syndrome, cleidocranial dysostosis, congenital anomalies of the skull and facial bones (missing skull bones, acrocephaly, deformity of the forehead, craniosynostosis, Crouzon's disease, hypertelorism, imperfections in skull fusion, oxycephaly, platybasia, premature cranial suture closure, tower skull, trigonocephaly), Ehleros-Danlos syndrome, Marfan syndrome, and congenital malformations that affect multiple body systems [25].

The most common craniofacial anomalies worldwide are cleft lip with or without cleft palate and craniosynostosis. This is reflected in the dataset where nearly 42% of the patients who underwent orthognathic surgery had cleft lip/palate, while 51% were diagnosed with a congenital anomaly of the skull or facial bones, such as craniosynostosis and Crouzon's syndrome. Just over half (50.6%) of the patients were female. The mean age at the time of surgery was 14.3 years (median 15.5 years). The average hospital charge per patient was $82,576 (median $48,786), amounting to $680.7 million total in six years. The average length of hospitalization is 6.8 days, but the median length of stay is 1.7 days. As is consistent with the literature that was previously discussed, private insurance paid for the majority (62.7%) of the surgeries, rather than Medicaid or Medicare [25].

The most common surgical complications include bacterial infections, hemorrhage, iatrogenic complications, and postoperative pneumonia. Other complications include decubitus ulcers, septicemia, mycoses, non-healing wounds, other infections, urinary complications, digestive system complications, nervous system complications, and cardiac complications. Despite complications, 7,923 patients (95%) were routinely discharged after surgery. In this sample, 78.5% of patients do not have a different comorbid condition, but those with a diagnosed comorbid burden have a higher risk of complications ($P<.05$). The most common comorbid conditions in this patient sample include chronic pulmonary disease, neurological disorders, deficiency anemia, valvular disease, hypertension, and hypothyroid. The most common complications (bacterial infections, hemorrhage, iatrogenic complications, and postoperative pneumonia) occur in at least 1% of the patients. These complications are more common in patients with comorbid conditions. The results of this study determine that patients with congenital craniofacial anomalies, including but not limited to cleft lip/palate, can safely undergo orthognathic surgery [25].

Comparatively, another retrospective study utilizing the Nationwide Inpatient Sample for all orthognathic surgeries from 2012-2013, supports the hypothesis that patients "with craniofacial anomalies have higher billed hospital charges, longer length of stay, and increased odds for developing infectious complications compared to those without craniofacial anomalies." These patients were divided into two groups: those with a craniofacial anomaly and those without a craniofacial anomaly. As in the previous study, these patients were identified based on the ICD-9-CM diagnosis codes and include, but are not limited to, patients with neurofibromatosis type 1, cleft lip/palate, acromegaly, congenital musculoskeletal deformities, Apert syndrome, Ehlers-Danlos, Marfan syndrome, craniosynostosis, Crouzon disease, etc. Of the 16,515 orthognathic surgeries performed during that year, 16.65% (2,750 patients) had a cleft lip/palate or craniofacial anomaly. Patients with craniofacial anomalies are more likely to undergo surgery on an emergent basis, 15.2% compared to only 5.5% of patients without a craniofacial anomaly. Patients with a craniofacial anomaly more frequently contract an infectious complication than those without an anomaly, 7.4% compared to 0.6%. The overall complication rate is also higher for patients with craniofacial anomalies than for those without, 10.7%

compared to 2.5% [37]. Multiple factors may play a role in the higher complication and infection rates for patients with craniofacial anomalies. For example, the urgency of the surgery may automatically increase the associated risks, which may contribute to the higher complication rates during and after surgery.

There are also differences in location and costs of surgery for patients with and without anomalies. Patients with craniofacial anomalies are more likely to be referred to specialized physicians or teaching hospitals. 91.7% of surgeries for patients with craniofacial anomalies occurred in a teaching hospital, while only 77.5% of patients without an anomaly had surgery in a teaching hospital.

Expenses for these surgeries are also dramatically different. The mean billed hospital charges for patients with a craniofacial anomaly is $83,128 more than for those without, $139,317 compared to $56,189. The mean length of hospital stay for patients with craniofacial anomalies is dramatically longer than for those without, 8.8 and 1.8 days respectively [37].

This study also noted that the older the patient is, the less likely the patient is to develop a bacterial infection, respiratory complication, or postoperative pneumonia [37]. This suggests that better outcomes may be achieved in older patients; however, these surgeries are time sensitive and later treatment is not always possible in cases of cleft lip/palate or craniofacial anomalies, where the mean age of the patient at the time of surgery is 13.8 years, compared to 25.3 years for those without an anomaly [25].

Even after adjusting for confounding variables such as age, gender, race, type of hospital admission, comorbidities, insurance status, hospital location, type, region, teaching status, number of procedures, and the year the surgery was performed, patients with a craniofacial anomaly are at significantly higher risk of developing infectious complications and at higher risk of developing one or more of any of the complications listed above [37]. The most common complications also differ between the two patient groups. The three most common complications in patients without craniofacial anomalies are iatrogenically induced complications (0.9%), hemorrhage (0.6%), and postoperative pneumonia (0.4%). Comparatively, the three most common complications in patients with craniofacial anomalies are bacterial infections (3.4%), postoperative pneumonia (3.1%), and iatrogenically induced complications (1.8%). Patients without an anomaly only have an infectious complication rate of 0.6% and an overall complication rate of 2.5%. This is significantly lower than for patients with craniofacial anomalies who have a bacterial infections rate and overall complication rate of 7.4% and 10.7% respectively [25].

The risk of infectious complications may be positively correlated to comorbid burden. Patients with comorbidities are more likely to be medically compromised and have higher risks associated with surgery. Also, patients with craniofacial anomalies are more likely to have a comorbid condition than those without craniofacial anomalies [25]. 76.5% of patients in this sample who did not have a craniofacial anomaly also did not have a comorbidity; while only 72.5% of patients with a craniofacial anomaly did not have a comorbid condition. Of the patients with a craniofacial anomaly, 16.7% had one comorbidity, 7.6% had two comorbidities, and 3.2% had three or more comorbidities. Comparatively, of those without a craniofacial anomaly 16.5%, 5.2%, and 1.8% of these patients had one, two, and three or more comorbidities respectively. Thus, the higher comorbidity rate in patients with a craniofacial anomaly may contribute to the higher rate of infectious complications than those patients without a craniofacial anomaly. It must be noted that the frequency and type of complication varies based on the surgical site, length of surgery, type of surgery, surgical approach, and wound contamination as well as the surgeon's skill and experience [25].

Skeletal disharmonies between the maxillae and the mandible can be corrected multiple ways including treating only the maxilla, only the mandible, or both the maxillae and the mandible. This may take place in one surgery or multiple surgeries. It is surprising to note that, despite having greater risk of complications, higher costs of surgery, and longer hospital stays, patients with craniofacial anomalies tend to have fewer surgical procedures performed than those without craniofacial anomalies. In patients without anomalies, 46.8% underwent only one procedure, while 42.2% and 11% of surgeries involved two procedures and three or more procedures respectively. Comparatively, over half (68.2%) of patients with craniofacial anomalies were treated with one surgery, while 25.4%, and 5.4% were treated with two and three or more surgeries, respectively [25].

According to the Nationwide Inpatient Sample there are 10,345 hospitalizations for orthognathic surgeries during 2008, but this study does not differentiate between patients with or without craniofacial anomalies. Rather, the purpose of this article is to report the demographics and types of surgical procedures performed in the United States. Of the 10,345 surgeries performed and reported in 2008, the majority of surgeries are due to a hypoplastic upper or lower jaw. 28.1% of patients are diagnosed as mandibular hypoplasia and 33.1% have maxillary hypoplasia; while treatment of maxillary and mandibular hyperplasias only account for 6.3% and 14% of surgeries, respectively. Depending on the magnitude of the jaw discrepancy, many patients may need a double jaw (maxillary and mandibular) surgery. In this nationwide sample, 53.3% of the surgeries consist of one procedure, 36.8% are two procedures, 9.2% are three procedures, and only 0.7% of the hospitalizations are four procedures. Congenital anomalies are relatively rare. Only 8.1% of the reported hospitalizations in this sample are due to congenital musculoskeletal deformities or anomalies of the facial bones and skeleton [14].

The most common complications seen in orthognathic surgical cases are similar to the ones noted in other studies: iatrogenically-induced (1.5%), hemorrhagic (1.2%), and bacterial infections (0.6%) [14]. The surgical outcomes, complication rates, length of hospital stay, costs of treatment, and access to care are important factors that require further consideration and research in order to improve patients' psychosocial and physical wellbeing.

Another study, evaluates cleft lip and palate patients before and after secondary alveolar bone grafting using Patient Reported Outcomes Measures (PROMs). 40 consenting cleft lip/palate patients ages 8-14 are included in this data. Half of these had and half did not have secondary alveolar bone grafts (SABG). According to the PROMs, there is no significant difference reported between patient and parents. Patients who underwent SABG did report significantly less nasal regurgitation and more nasal obstruction than those who did not undergo SABG [26].

One literature review was found that summarizes the recent evidence based literature on the outcomes of cleft lip/palate treatments. Treatment modalities include nasoalveolar molding, speech outcomes related to palatoplasty timing, technique, and intravelar veloplasty. These studies investigate the relationship between palatoplasty timing and facial development.

The literature reviewed does not include evidence to support a superior method of cleft lip repair, but it is noted that most surgeons in North America utilize a rotation-advancement approach and perform cleft rhinoplasty at the time of primary lip repair; this is to decrease the number of revision surgeries needed long term. At 9-12 months of age, most surgeons perform a single stage palatoplasty to improve early speech. There is not enough existing evidence to support a two-stage palatoplasty. Further research is necessary, but it is difficult due to lack of validated cleft-specific outcome measurement tools [33]. This literature review does not include surgical outcomes or risks involved in this treatment for patients with cleft lip/palate. Thus, further research on this topic is necessary.

A study of 4,571 patients with cleft lip/palate states that these patients experience a high rate of hospital-based care early in life [30]. Within 30 days of surgery, patients with cleft palate are likely to return to the hospital. This study supports previous literature mentioned that cleft lip/palate patients also have higher associated hospital charges than non-cleft patients [30]. The initial diagnosis (such as cleft lip/palate) and the patient's age at surgery are the most important factors that increase costs of treatment as well as increase frequency of hospital visits. Patients with cleft lip and palate are most likely to visit the hospital and have higher hospital charges. Comparatively, patients with cleft lip without cleft palate have fewer hospital visits and lower hospital-associated costs [30]. The patients' age at the time of surgery also influences the chance of complications. Cleft lip repair in neonates is associated with a higher rate of complication, longer length of hospitalization, and increased hospital charges compared to if the cleft lip repair is performed when the baby is 3-4 months old [29]. The benefits of cleft lip repair in neonates may not outweigh the associated risks.

From these results, we can interpret that it is important to streamline hospital policies in order to decrease failures and improve treatment outcomes for cleft lip and palate patients.

HYPOTHESIS AND AIMS

Specific Aim 1: The purpose of this study is to examine the prevalence of adverse effects of medical care and infectious complications in patients with cleft lip/palate undergoing facial bone repairs and/or orthognathic surgeries.

Specific Aim 2: The other goal of this study is to evaluate how adverse events affect hospital charges and length of hospital stay.

Hypothesis: We predict that there is a combination of patient and hospital level factors that contribute to the occurrence of these adverse events and that the occurrence of these events is associated with substantial increases in hospital charges and length of hospitalization.

MATERIALS AND METHODS

Database*:* The Nationwide Inpatient Sample (NIS) for the years 2012 to 2014 was used for the current study. The NIS is a 20% stratified probability sample of hospitalizations occurring in all acute care hospitals in the United States and is a component of the Healthcare Cost and Utilization Project (HCUP) sponsored by the Agency for Healthcare Research and Quality (AHRQ) [12]. Each hospital in the NIS sample provide information on 20% of hospitalizations occurring during the select years. Each hospitalization is then assigned a sampling weight taking into account the hospital stratum from which it is drawn. Hospital stratification is based on location of hospital, geographic region of hospital, bed size, teaching status, and ownership/control. The discharge weight variable can be used to provide nationally representative estimates of all hospitalizations and associated outcomes occurring in the United States. The NIS provides information on several patient level variables including age, sex, race, insurance status, primary reason for hospitalizations, comorbid burden, external causes of injuries, procedures performed during hospitalization, type of admission, disposition status, hospitalization charges, and length of stay in hospital.

Data user agreement*:* One of the authors contacted HCUP-AHRQ and completed a data user agreement to use the NIS databases. According to the data user agreement, individual cell counts <=10 cannot be reported (to preserve patient confidentiality). The term "DS" (Discharge-information Suppressed) has been used when presenting such low counts in the current study. The study was exempt from Institutional Review Board approval.

Case selection*:* All patients with a diagnosis of cleft lip/palate (based on ICD-9-CM diagnosis codes) that had a facial bone repair or orthognathic surgery were selected for analysis. Selection of procedures was based on ICD-9-CM procedure codes. The codes included: Closed osteoplasty/osteotomy of mandibular ramus (ICD-9-CM procedure code of 76.61), open osteoplasty/osteotomy of mandibular ramus (76.62), osteoplasty/osteotomy of body of mandible (76.63), other orthognathic surgery on mandible (76.64), segmental osteoplasty/osteotomy of maxilla (76.65), total osteoplasty /osteotomy of maxilla (76.66), reduction genioplasty (76.67), augmentation genioplasty (76.68), and other facial bone repair (76.69). The ICD-9-CM diagnosis codes used for identifying cleft lip/palate included: Cleft palate, unspecified - 749.00; Cleft palate, Unilateral complete - 749.01; Cleft palate, Unilateral incomplete (cleft uvula) - 749.02; Cleft palate, Bilateral complete - 749.03; Cleft palate, Bilateral incomplete - 749.04; Cleft lip, unspecified - 749.10; Cleft lip, Unilateral complete - 749.11; Cleft lip, Unilateral incomplete - 749.12; Cleft lip, Bilateral complete - 749.13; Cleft lip, Bilateral incomplete - 749.14; Cleft palate with cleft lip, unspecified - 749.20; Cleft palate with cleft lip, Unilateral complete - 749.21; Cleft palate with cleft lip, Unilateral incomplete - 749.22; Cleft palate with cleft lip, Bilateral complete - 749.23; Cleft palate with cleft lip, Bilateral incomplete - 749.24; Cleft palate with cleft lip, and Other combinations - 749.25.

Variables of Interest*:* The following sections provide an overview of the variables of interest in the present study. Broadly, these included patient demographics, hospital characteristics, and outcomes (adverse effects of medical care, infectious complications, hospital charges, and length of stay).

Patient Demographics: The demographic characteristics of interest included: age of patient (in years at time of admission), sex, race (White, Black, Hispanic, Asian/Pacific Islander, Native Americans, and Other Races), type of admission (elective admission versus emergency/urgent admission), insurance status (covered by Medicare, Medicaid, private insurance plans, or other insurance plans), co-morbid burden, types of cleft lip/palate (identified by ICD-9-CM diagnoses codes in all diagnostic fields), procedures performed during hospitalization, and year of hospitalization. For estimating the co- morbid burden, the NIS co-morbid severity files were examined. The occurrence of 29 different co-morbid conditions (AIDS, Alcohol abuse, Deficiency anemias, Rheumatoid arthritis/collagen vascular diseases, Chronic blood loss anemia, Congestive heart failure, Chronic pulmonary disease, Coagulopathy, Depression, Diabetes – uncomplicated, Diabetes with chronic complications, Drug abuse, Hypertension, Hypothyroidism, Liver disease, Lymphoma, Fluid and electrolyte disorders, Metastatic cancer, Other neurological disorders, Obesity, Paralysis, Peripheral vascular disorders, Psychoses, Pulmonary circulatory disorders, Renal failure, Solid tumor without metastasis, Peptic ulcer disease: excluding bleeding, Valvular disease, and Weight loss) was examined. A co-morbid burden score was computed by summing up the occurrences of each co- morbid condition.

Hospital Characteristics*:* The hospital characteristics examined included: hospital geographic region (Northeast, Midwest, South, or West), hospital bed size into small, medium, or large bed sized hospitals depending on the number of beds in the hospital by geographic region and urban/rural status), and hospital location/teaching status of hospital (Rural hospital, Urban non-teaching hospital, or Urban teaching hospital).

Adverse effects of medical care: The NIS database has 4 variable fields dedicated to capture information on "causes of injuries" (E-codes). Injury codes for "Adverse effects of medical care" were used in the E-code fields to assess the different types of adverse effects that occurred due to medical care. The codes used included: Accidental cut, puncture, perforation, or hemorrhage during medical care (Injury code of E870); Foreign object left in body during procedure (E871); Failure of sterile precautions during procedure (E872); Failure in dosage (E873); Mechanical failure of instrument or apparatus during procedure (E874); Contaminated or infected blood, other fluid, drug, or biological substance (E875); Other and unspecified misadventures during medical care (E876); Surgical operation and other surgical procedures as the cause of abnormal reaction of patient, or of later complication, without mention of misadventure at the time of operation (E878); Other procedures, without mention of misadventure at the time of procedure, as the cause of abnormal reaction of patient, or of later complication (E879).

Infectious Complications: The NIS database provides information on primary diagnosis and 29 different secondary diagnoses fields which can be examined for occurrence of any medical complication occurring during hospitalization. The infectious complications that were examined included: Septicemia, bacterial infections, mycoses, and pneumonia.

These infectious events were identified using Clinical Classification Software codes in the secondary diagnoses fields. The Clinical Classification Software system groups' clusters of ICD-9-CM diagnosis codes together to group closely related conditions [44]. Over 500 ICD-9-CM diagnoses codes were used to identify the infectious events. A composite variable designated "Infectious Complication" was created based on if a patient had any of the relevant infectious event.

Hospital Charges: This refers to the amount charged by the hospitalizations. Since three years of data was used, the charges were adjusted to year 2014 $ value using the Bureau of Labor Statistics inflation levels for hospital care [45]. The hospital charges were highly skewed and hence were log transformed.

Length of Stay: This refers to the number of days a patient was hospitalized during the index admission. The length of stay data was highly skewed and hence was log transformed.

Analytical approach*:* Descriptive statistics were used to summarize the data. The primary outcome of interest included the occurrence of at least one adverse effect of medical care event during hospitalization, occurrence of at least one infectious complications, hospital charges, and length of stay in hospital. The adverse effect of medical care event was used as binomial variables (Yes: Had an adverse effect of medical care; No: Did not have an adverse effect). In a similar fashion, the occurrence of infectious complications was also used as a binomial variable (Yes: Developed an infectious complication; No: Did not develop infectious complication. The independent variables of interest included age (every 1 year increase), sex, race, insurance status (uninsured versus all other insurance plans), type of procedure a patient had during hospitalization (maxillary procedure versus other procedures), co-morbid burden (each one unit increase), hospital region, and type of admission. The association between the outcome variable and independent variables was examined by a multivariable logistic regression model. Odds ratios (for having an adverse medical effect and infectious complications) and associated 95% confidence intervals were computed for each level of independent variable. For hospital charges and length of stay, multivariable linear regression models were used. The hospital charges and length of stay were modeled as continuous variables following log transformation. In these models, occurrence of adverse effect of medical care and occurrence of infectious complications were the primary independent variables. The effects of confounders such as age, sex, race, insurance status, type of procedure, co-morbid burden, hospital region, and type of admission were adjusted. Parameter estimates and 95% confidence intervals were computed for each level of independent variables. The parameter estimates were re-transformed to compute mean changes in hospital charges and length of stay. All tests were two-sided and a p-value of <0.05 was deemed to be statistically significant. Each individual hospitalization was the unit of analysis and the hospital stratum was used as the stratification unit. The effects of clustering of outcomes within hospitals was adjusted in the multivariable regression model. Variances were computed Taylor Linearization methods in all multivariable models. All statistical analyses were conducted using SAS version 9.3 software (SAS Institute, Cary, NC) and SUDAAN 11.0.3 (Research Triangle Park, NC).

RESULTS

During the study period a total of 1,785 patients with cleft lip/palate had a facial bone repair/ orthognathic surgical procedure in the United States. Patient characteristics are outlined in Table 1. Close to 48% of patients were female. White race was the predominating (60.4%) followed by Hispanics (21.1%), Asians/Pacific Islanders (6.4%), Blacks (5.7%), other races/more than one race (5.4%), and Native Americans (1%). The major payer were private insurance plans accounting for 57.4% of patients. Medicaid accounted for 34.5% of patients. 4.8% of patients were uninsured. 21% of patients had at least one of the 29 co-morbid conditions examined in the present study. The five most frequently reported co-morbid conditions were fluid and electrolyte disorders (6.2%), deficiency anemias (4.2%), chronic pulmonary disease (3.9%), hypertension (2.2%), and depression (1.7%). A vast majority of patients (70%) underwent the procedures on an elective basis. The distribution of age is presented in figure 1. Age had an obvious bimodal distribution with 34% of them aged <1 year (likely to be those requiring early distractions for air way issues) and close to 50% of patients aged between 15 years and 21 years (likely the cohort that required an orthognathic surgery for skeletal malocclusions). The overall mean age was 11.4 years (median age was 15.1 years).

The different types of clefts are summarized in table 2. Cleft palate – unspecified was the most frequently coded condition (33.9%) followed by cleft palate with cleft lip – unspecified (15.4%), cleft palate with cleft lip – unilateral incomplete (13.2%), cleft palate with cleft lip – bilateral incomplete (10.6%), and cleft palate with cleft lip – unilateral complete (10.1%). The different types of surgical procedures are summarized in table 3. Overall, surgical procedures in the mandible (47.9%) and maxilla (55.5%) greatly outnumbered genioplasty (7%). The frequently performed surgical procedures included: segmental osteoplasty of maxilla (39.8%), other orthognathic surgery on mandible (30%), open osteoplasty of ramus (16.8%), total osteoplasty of maxilla (15.7%), and other facial bone repair (11.5%).

Hospital characteristics are presented in table 5. Southern regions of the country accounted for 33% of all patients while Western (26.3%), Midwestern (24.7%), and Northeastern (16%) regions accounted for the rest. A vast majority of procedures (98%) were performed in urban teaching hospitals with none reported to be performed in rural hospitals. Large bed size hospitals performed 50.4% of all procedures.

The disposition status of patients following the surgical procedures are presented in table 5. Over 90% of patients were discharged routinely following the surgical procedure while 7.4% were discharged to a home health care facility and 2% were transferred to another short term care facility.

Close to 8% of patients developed an infectious complication (table 6). Bacterial infections occurred in 3.4% of patients while pneumonia occurred in 2.2%, mycoses occurred in 2.2%, and septicemia occurred in 2% of patients. At least one adverse effect of medical care occurred in 10.4% of patients (Table 7). In 8.7%, surgical operation and procedures caused abnormal reaction of patient or complication. Other procedures, including but not limited to cardiac catherization, kidney dialysis, radiological procedure and radiotherapy, led to abnormal reaction or complications in 1.1%. 0.8% of patients experienced an accidental cut, puncture, perforation, or hemorrhage during medical care.

Other misadventures during medical care, such as mismatched blood in transfusion, wrong fluid in infusion, failure in suture, did not occur in this cohort. There were no cases with foreign object left in body during procedure or mechanical failure of instrument during procedure. There were no cases of failure of sterile precautions during procedure, failure in dosage, and contaminated or infected blood, fluid, drug or biological substance.

The distribution of hospital charges and length of stay are presented in table 8, figure 2, and figure 3. The mean hospitalization charge was $168,473 and median charge was $75,949. The total hospitalization charges across the entire United States was over $292 million. The average length of stay in hospital was 14.4 days and the median was 2.1 days. The total hospitalization days across the entire United States was 25,650 days. Both hospital charges and length of stay were highly skewed.

The results of the multivariable logistic regression analysis examining the association between adverse occurrence of infectious complication (outcome) and the independent variables are summarized in table 9. The odds of having an infectious complication was significantly higher for “other races/mixed races” compared to Whites (odds ratio [OR]=7.29, 95% confidence interval [CI] = 1.38 – 38.63, p=0.02), even after controlling for other variables. Those who underwent the procedures of an elective basis had a lower odds for developing an infectious complication compared to those who underwent the procedure on an emergency/urgent basis (OR = 0.06, 95% CI = 0.01 – 0.25, p<0.001). Each one unit increase in co-morbid burden was associated with increased odds for developing infectious complications (OR = 1.94, 95% CI = 1.12 – 3.37, p=0.02).

The results of the multivariable logistic regression analysis examining the association between adverse effects of medical care (outcome) and the independent variables are summarized in table 10. The odds of having an adverse effect of medical care was significantly higher for Hispanics compared to Whites (OR=2.75, 95% CI = 1.07 – 7.10, p=0.04), even after controlling for other variables. “Other/Mixed races” also were associated with higher odds for having adverse effects of medical care compared to Whites (OR = 8.01, 95% CI = 1.79 – 36, p=0.007). Those who underwent the procedures of an elective basis had a lower odds for having adverse effect of medical care compared to those who underwent the procedure on an emergency/urgent basis (OR = 0.24, 95% CI = 0.06 – 0.90, p=0.03).

The results of the multivariable linear regression model examining the impact of having an adverse effect of medical care and developing infectious complications on hospital charges is summarized in table 11. After controlling for all other available confounders, those who had an adverse effect of medical care were associated with significantly higher hospital charges (Parameter estimate = 0.3161, $62,633 higher charge than mean, 95% CI for parameter estimate = 0.0443 – 0.5879, p = 0.02) when compared to those who did not have an adverse effect of medical care. Similarly, those who developed an infectious complication were associated with significantly higher hospital charges (Parameter estimate = 0.5481, $122,979 higher charge than mean, 95% CI for parameter estimate = 0.2450 – 0.8511, p = 0.0005) when compared to those who did not develop an infectious complication. Other significant factors associated with hospital charges included age (-$3,270 for each 1 year increase in age, p = 0.006), procedures in the maxilla (-$80,926, p<0.0001), elective admissions (-$74,494, p<0.0001), and Midwest regions (-$36,672, p=0.02). The multivariable regression model R^2 value was 0.6314 indicating that close to 63% of variance in hospital charges can be explained by the predictor variables used in the model.

The results of the multivariable linear regression model examining the impact of having an adverse effect of medical care and developing infectious complications on length of stay is summarized in table 12. After controlling for all other available confounders, those who had an adverse effect of medical care were not associated with significantly longer length of stay in hospital when compared to those who did not have an adverse effect of medical care. Those who developed an infectious complication were associated with significantly longer length of stay in hospital (Parameter estimate = 0.7236, 15.3 days higher charge than mean, 95% CI for parameter estimate = 0.3770 – 1.0703, p = 0.0001) when compared to those who did not develop an infectious complication. Other significant factors associated with length of stay in hospital included age (-0.6 days for each 1 year increase in age, p = 0.0008), procedures in the maxilla (-7.5 days, p=0.0001), and elective admissions (-10.1 days, p<0.0001). The multivariable regression model R^2 value was 0.7513 indicating that close to 75% of variance in length of stay can be explained by the predictor variables used in the model.

Table 1. Characteristics of Patients with Cleft Lip/Palate undergoing Facial Repairs/Orthognathic surgical procedures in 2012-2014 in the United States.

Characteristics	N = 1785
Gender	
Male	52.1%
Female	47.9%
Race	
White	60.4%
Black	5.7%
Hispanic	21.1%
Asian/Pacific Islanders	6.4%
Native Americans	1%
Other Races	5.4%
Insurance	
Medicare	DS
Medicaid	34.5%
Private	57.4%
Uninsured	4.8%
Other insurance	3.1%
Comorbid Condition Burden	
AIDS	0
Alcohol abuse	0.8%
Deficiency anemias	4.2%
Rheumatoid arthritis/collagen vascular diseases	0%
Chronic blood loss anemia	DS
Congestive heart failure	0
Chronic pulmonary disease	3.9%
Coagulopathy	1.1%
Depression	1.7%
Diabetes – uncomplicated	DS
Diabetes with chronic complications	0
Drug abuse	1.1%
Hypertension	2.2%
Hypothyroidism	DS
Liver disease	DS
Lymphoma	0
Fluid and electrolyte disorders	6.2%
Metastatic cancer	0
Other neurological disorders	0.8%
Obese	DS
Paralysis	DS
Peripheral vascular disorders	0

Table 1 - continued	
Psychoses	1.1%
Pulmonary circulatory disorders	0.8%
Renal failure	DS
Solid tumor without metastasis	DS
Peptic ulcer disease: excluding bleeding	0
Valvular disease	1.4%
Weight loss	0.8%
Comorbid burden	
0	79%
1	14.8%
2	4.2%
>=3	2%
Year of Hospitalization	
2012	34.4%
2013	30%
2014	35.6%
Admission	
Urgent	30%
Elective	70%

DS: Discharge information suppressed as per AHRQ data user agreement (cell counts <=10 cannot be reported)
Individual cell counts will not add to the total global cell count because of missing values

Figure 1. Distribution of Age of Patients

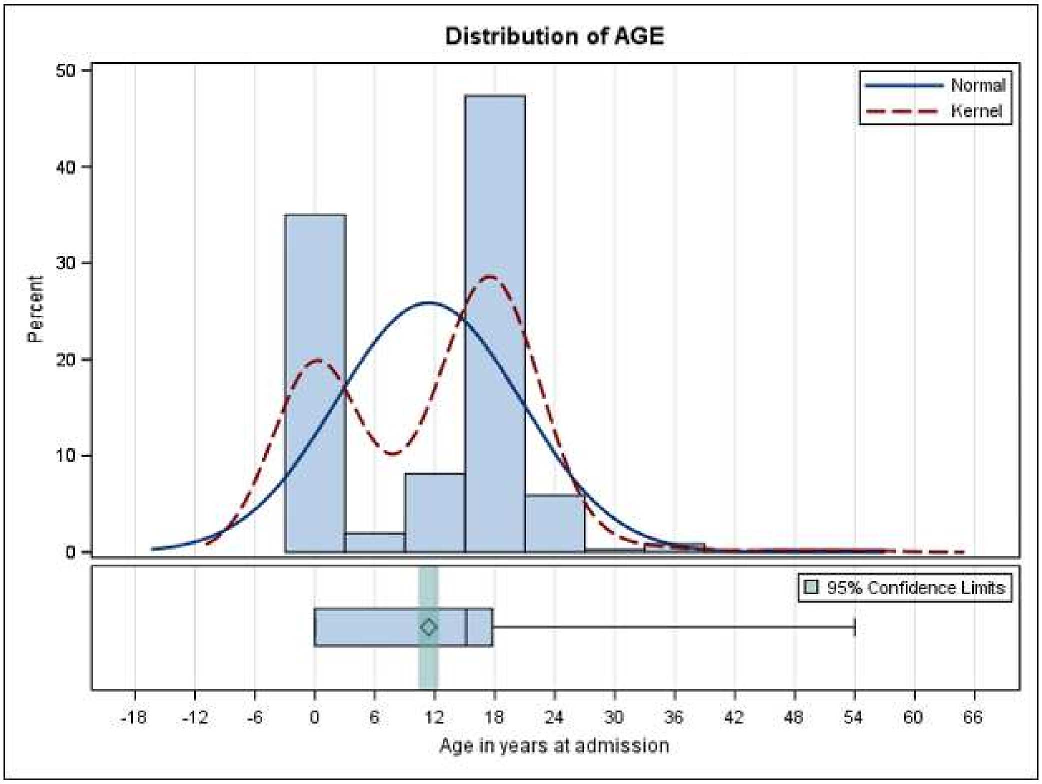

Table 2. Types of Cleft Lip/Palate

Type of Cleft Lip/Palate (ICD-9-CM Diagnosis Code)	N = 1785
Cleft palate, unspecified - 749.00	33.9%
Cleft palate, Unilateral complete - 749.01	DS
Cleft palate, Unilateral incomplete (cleft uvula) - 749.02	2%
Cleft palate, Bilateral complete - 749.03	1.1%
Cleft palate, Bilateral incomplete - 749.04	3.1%
Cleft lip, unspecified - 749.10	0.8%
Cleft lip, Unilateral complete - 749.11	DS
Cleft lip, Unilateral incomplete - 749.12	0
Cleft lip, Bilateral complete - 749.13	0
Cleft lip, Bilateral incomplete - 749.14	0.5%
Cleft palate with cleft lip, unspecified - 749.20	15.4%
Cleft palate with cleft lip, Unilateral complete - 749.21	10.1%
Cleft palate with cleft lip, Unilateral incomplete - 749.22	13.2%
Cleft palate with cleft lip, Bilateral complete - 749.23	7.8%
Cleft palate with cleft lip, Bilateral incomplete - 749.24	10.6%
Cleft palate with cleft lip, Other combinations - 749.25	1.1%

DS: Discharge information suppressed as per AHRQ data user agreement (cell counts <=10 cannot be reported)

Individual cell counts will not add to the total global cell count because a patient can present with more than one type of cleft and missing values

Table 3. Types of Procedures

Type of Procedures (ICD-9-CM Procedure Code)	N = 1785
Closed osteoplasty [osteotomy] of mandibular ramus, 76.61	DS
Open osteoplasty [osteotomy] of mandibular ramus, 76.62	16.8%
Osteoplasty [osteotomy] of body of mandible, 76.63	5.6%
Other orthognathic surgery on mandible, 76.64	30%
Segmental osteoplasty [osteotomy] of maxilla, Maxillary osteoplasty, 76.65	39.8%
Total osteoplasty [osteotomy] of maxilla, 76.66	15.7%
Reduction genioplasty, 76.67	0.8%
Augmentation genioplasty, 76.68	6.2%
Other facial bone repair, 76.69	11.5%
Procedure of Mandible	47.9%
Procedure of Maxilla	55.5%
Procedure involving Genio	7%

DS: Discharge information suppressed as per AHRQ data user agreement (cell counts <=10 cannot be reported)
Individual cell counts will not add to the total global cell count because a patient can have more than one procedure and missing values

Table 4. Hospital Characteristics

Hospital Characteristics		N = 1785
Hospital Region	Northeast	16%
	Midwest	24.7%
	South	33%
	West	26.3%
Hospital Location/Teaching Status	Rural hospital	0
	Urban non-teaching hospital	2%
	Urban teaching hospital	98%
Hospital bed size	Small	16.8%
	Medium	32.8%
	Large	50.4%

Table 5. Disposition Status of Patient following Surgery

Disposition Status	N = 1785
Routine discharge	90.5%
Transferred to another short term hospital	2%
Other transfers - Includes Skilled Nursing Facility (SNF), Intermediate Care Facility (ICF), Another Type of Facility	DS
Home Health Care	7.3%

DS: Discharge information suppressed as per AHRQ data user agreement (cell counts <=10 cannot be reported)

Table 6. Types of Infectious Complications

Disposition Status	N = 1785
Septicemia	2%
Bacterial infections	3.4%
Mycoses	2.2%
Pneumonia	2.2%
Any of above infectious complications	8.1%

Table 7. Types of Adverse Effects of Medical Care (AEMC).

AEMC (External Cause of Injury Code)	N = 1785
Accidental cut, puncture, perforation, or hemorrhage during medical care (E870)	0.8%
Foreign object left in body during procedure (E871)	0
Failure of sterile precautions during procedure (E872)	0
Failure in dosage (E873)	0
Mechanical failure of instrument or apparatus during procedure (E874)	0
Contaminated or infected blood, other fluid, drug, or biological substance (E875)	0
Other and unspecified misadventures during medical care (E876): Includes – • Mismatched blood in transfusion • Wrong fluid in infusion • Failure in suture and ligature during surgical operation • Endotracheal tube wrongly placed during anesthetic procedure • Failure to introduce or to remove other tube or instrument • Performance of inappropriate operation • Other specified misadventures during medical care • Performance of inappropriate treatment NEC • Unspecified misadventure during medical care	0
Surgical operation and other surgical procedures as the cause of abnormal reaction of patient, or of later complication, without mention of misadventure at the time of operation (E878) Includes: • Surgical operation with implant of artificial internal device • Surgical operation with anastomosis, bypass, or graft, with natural or artificial tissues used as implant • Surgical operation with formation of external stoma • Other restorative surgery • Amputation of limb(s) • Removal of other organ (partial) (total) • Other specified surgical operations and procedures • Unspecified surgical operations and procedures	8.7%
Other procedures, without mention of misadventure at the time of procedure, as the cause of abnormal reaction of patient, or of later complication (E879)	1.1%
Any of the above	10.4%

Note: Individual cell counts will not add up to the global totals since a hospitalization may experience one or more types of medical injuries.
DS: Discharge information suppressed as per AHRQ data user agreement (cell counts <=10 cannot be reported)

Table 8. Hospital Charges and Length of Stay in Hospital

Outcome	Mean	Standard Error of Mean	Median	Total Across Entire USA
Hospital Charges*	$168,473	12,156	$75,949	$292,300, 627
Length of Stay in Days	14.4	1.26	2.1	25,650

*Hospital charges adjusted to year 2014 $ value using Bureau of Labor Statistics inflation estimates for hospital care.

Figure 2. Distribution of Hospital Charges

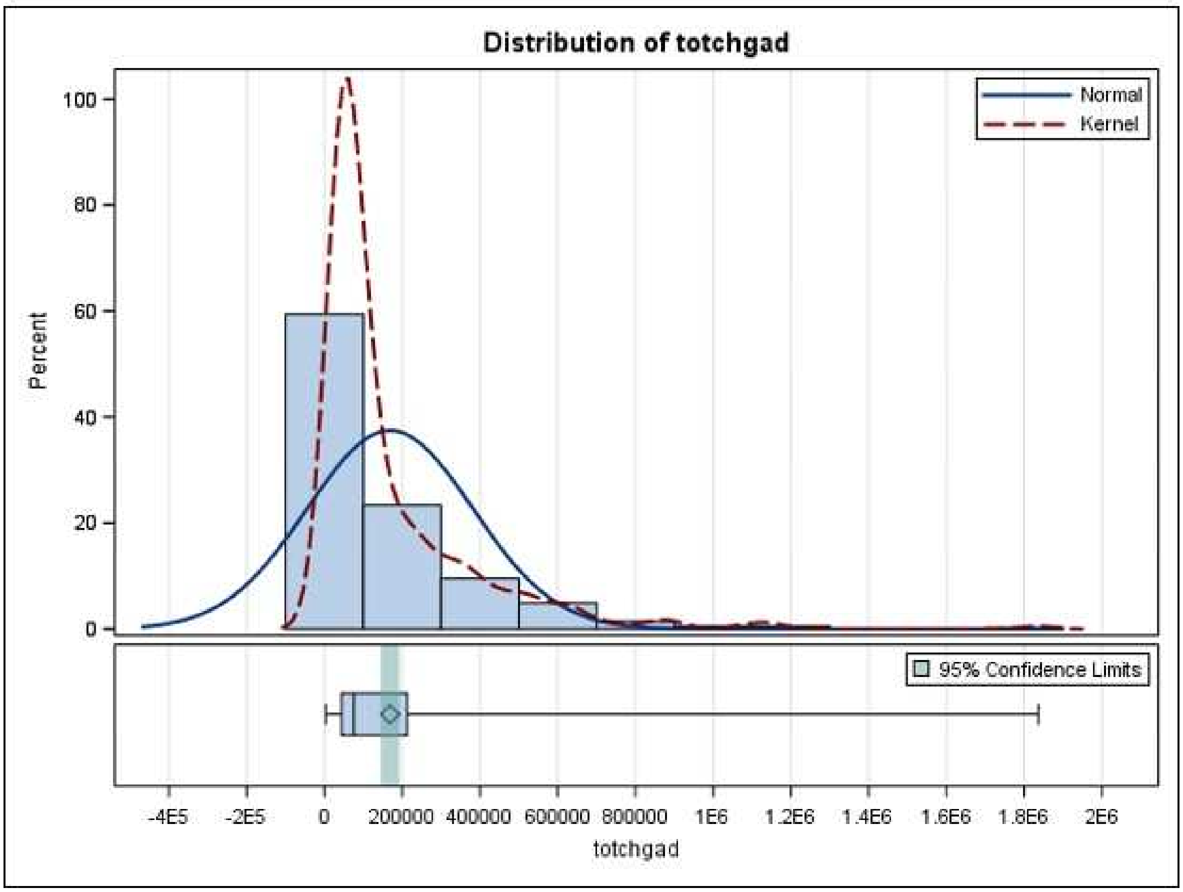

Figure 3. Distribution of Length of Stay in Hospital

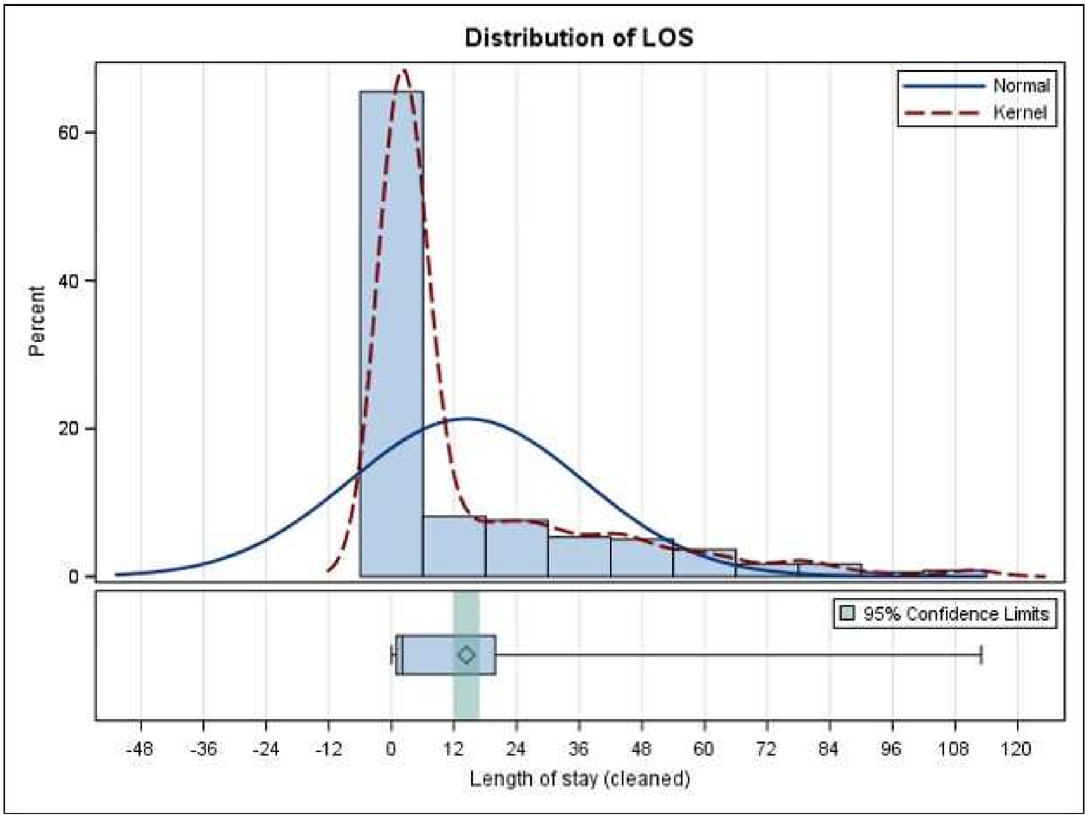

Table 9. Multivariable Logistic Regression Analysis – Infectious Complications as an Outcome.

Characteristic		Odds Ratio (95% CI)	p-value
Age in years	1 year increase	1.05 (0.93 – 1.18)	0.47
Sex	Female	2.29 (0.73 – 7.15)	0.15
	Male	Reference	
Race	Black	2.61 (0.59 – 11.58)	0.20
	Hispanic	3.30 (0.97 – 11.23)	0.06
	Asian/Pacific Islander	1.11 (0.15 – 8.51)	0.92
	Native American	0.00	-
	Other race	7.29 (1.38 – 38.63)	0.02
	White	Reference	
Insurance	Uninsured	0.00	-
	All others	Reference	
Procedure	Procedure in Maxilla	0.16 (0.02 – 1.55)	0.11
	All others	Reference	
Type of admission	Elective	0.06 (0.01 – 0.25)	<0.001
	Emergency/Urgent	Reference	
Co-morbid burden	Each 1 unit increase	1.94 (1.12 – 3.37)	0.02
Hospital region	Northeast	1.78 (0.42 – 7.48)	0.43
	Midwest	0.70 (0.15 – 3.22)	0.65
	South	0.70 (0.20 – 2.50)	0.58
	West	Reference	

*= p-value is <0.05 (deemed to be statistically significant. All tests are two-sided)

Table 10. Multivariable Logistic Regression Analysis - Adverse Effects of Medical Care as an Outcome.

Characteristic		Odds Ratio (95% CI)	p-value
Age in years	1 year increase	0.96 (0.90 – 1.03)	0.29
Sex	Female	1.35 (0.59 – 3.08)	0.48
	Male	Reference	
Race	Black	1.60 (0.38 – 6.78)	0.52
	Hispanic	2.75 (1.07 – 7.10)	0.04
	Asian/Pacific Islander	0.65 (0.07 – 5.91)	0.70
	Native American	6.25 (0.17 – 223.4)	0.31
	Other race	8.01 (1.79 – 36)	0.007
	White	Reference	
Insurance	Uninsured	0.98 (0.11 – 8.62)	0.98
	All others	Reference	
Procedure	Procedure in Maxilla	2.42 (0.67 – 8.69)	0.17
	All others	Reference	
Type of admission	Elective	0.24 (0.06 – 0.90)	0.03
	Emergency/Urgent	Reference	
Co-morbid burden	Each 1 unit increase	1.21 (0.63 – 2.32)	0.56
Hospital region	Northeast	0.78 (0.23 – 2.67)	0.69
	Midwest	0.80 (0.26 – 2.43)	0.69
	South	0.66 (0.25 – 1.77)	0.41
	West	Reference	

*= p-value is <0.05 (deemed to be statistically significant. All tests are two-sided)

Table 11. Multivariable Linear Regression Analysis – Hospital Charges (Log Transformed) as an Outcome.

Characteristic		Parameter Estimate	$ Change from Mean	95% CI	p-value
Had a Medical Injury	Yes	0.3161	$62,633	0.0443 – 0.5879	0.02
	No	Reference			
Developed Infectious Complications	Yes	0.5481	$122,979	0.2450 – 0.8511	0.0005
	No	Reference			
Age in years	1 year increase	-0.0196	-$3,270	-0.0335 - -0.0057	0.006
Sex	Female	-0.0106	-$1,776	-0.1424 – 0.1212	0.87
	Male	Reference			
Race	Black	0.1504	$27,343	-0.1758 – 0.4766	0.36
	Hispanic	0.0249	$4,248	-0.1705 – 0.2202	0.80
	Asian/Pacific Islander	-0.0934	-$15,023	-0.3899 – 0.2031	0.53
	Native American	0.0932	$16,457	-0.5163 – 0.7027	0.76
	Other race	-0.1286	-$20,330	-0.6338 – 0.3766	0.62
	White	Reference			
Insurance	Uninsured	-0.1985	-$30,332	-0.5909 – 0.1939	0.32
	All others	Reference			
Procedure	Procedure in Maxilla	-0.6546	-$80,926	-0.8916 - -0.4175	<0.0001
	All others	Reference			
Type of Admission	Elective	-0.5837	-$74,494	-0.8600 - -0.3074	<0.0001
	Emergency/ Urgent	Reference			

Table 11-Continued					
Co-morbid burden	Each 1 unit increase	0.1020	$18,091	-0.0162 – 0.2202	0.09
Hospital region	Northeast	-0.1465	-$22,958	-0.3801 – 0.0871	0.22
	Midwest	-0.2531	-$37,672	-0.4690 - -0.0372	0.02
	South	-0.0316	-$5,240	-0.2009 – 0.1377	0.71
	West	Reference			

*= p-value is <0.05 (deemed to be statistically significant. All tests are two-sided)
R^2 value for this model was 0.6314

Table 12. Multivariable Linear Regression Analysis – Length of Stay in Hospital (Log Transformed) as an Outcome.

Characteristic		Parameter Estimate	Change in Days from Mean	95% CI	p-value
Had a Medical Injury	Yes	0.2296	3.7	-0.0571 – 0.5163	0.12
	No	Reference			
Developed Infectious Complications	Yes	0.7236	15.3	0.3770 – 1.0703	0.0001
	No	Reference			
Age in years	1 year increase	-0.0408	-0.6	-0.0643 - -0.0172	0.0008
Sex	Female	-0.0374	-0.5	-0.2093 – 0.1344	0.67
	Male	Reference			
Race	Black	0.0518	0.8	-0.2508 – 0.3545	0.74
	Hispanic	0.0339	0.5	-0.1733 – 0.2411	0.75
	Asian/Pacific Islander	-0.1257	-1.7	-0.4478 – 0.1965	0.44
	Native American	0.5399	10.3	-0.0875 – 1.17	0.09
	Other race	0.0487	0.7	-0.3773 – 0.4746	0.82
	White	Reference			
Insurance	Uninsured	-0.2343	-3	-0.6677 – 0.1991	0.29
	All others	Reference			
Procedure	Procedure in Maxilla	-0.7321	-7.5	-1.0835 - -0.3807	0.0001
	All others	Reference			
Type of admission	Elective	-1.2167	-10.1	-1.6215 - -0.8120	<0.0001
	Emergency/ Urgent	Reference			

Table 12 – Continued					
Co-morbid burden	Each 1 unit increase	0.1162	1.8	-0.0081 – 0.2404	0.07
Hospital region	Northeast	-0.0448	-0.6	-0.3742 – 0.2847	0.79
	Midwest	-0.1352	-1.8	-0.3737 – 0.1034	0.26
	South	0.0887	1.3	-0.1259 – 0.3032	0.42
	West	Refer ence			

*= p-value is <0.05 (deemed to be statistically significant. All tests are two-sided)

R^2 value for this model was 0.7513

DISCUSSION

To our knowledge, very few studies have provided nationally representative estimates of outcomes in patients with cleft lip/palate having orthognathic surgeries across the entire United States and none of these studies have examined adverse effects of medical care or infectious complication events during hospitalization [13, 14]. The current study provides nationally representative estimates of hospitalization outcomes among those with cleft lip/palate having facial bone repair and orthognathic surgeries in the United States over a three year period from 2012 to 2014. The results of the current study indicated that adverse effects of medical care occur in about 10.4% of patients with cleft lip/palate having facial bone repairs and orthognathic surgeries. Infectious complications occurred in 8.1% of patients. A comprehensive set of patient related factors that were available in the NIS database were used to identify risk factors associated with the occurrence of adverse effects of medical care during hospitalization. Results of our study suggest that those undergoing the procedures on an elective basis were associated with lower odds for experiencing an adverse effect of medical care or developing an infectious complication. "Other/Mixed races" were associated with higher risks for experiencing an adverse effect due to medical care and developing an infectious complication when compared to Whites. Hispanics were also associated with higher risk for experiencing an adverse effect due to medical care when compared to Whites. The risk of an infectious complication increased with increase in co-morbid burden. The Institute of Medicine reported that close to 45,000 deaths occur in hospital settings due to medical errors [15]. The Center for Medicare Services no longer reimburses hospitals for treating conditions occurring due to medical errors [16]. Zhan and Miller estimated that close to $9 billion is being spent annually for treating patient safety events that are presumed to occur due to medical errors in hospitals [17]. Consistent with this prior finding, our study also demonstrated that occurrence of an adverse effect of medical care is associated with substantial increases in hospital charges.

Prior studies have shown that life threatening complications following orthognathic surgeries are rare and orthognathic surgeries are considered to be safe [18, 19]. In this present study cohort, no mortalities were reported. Prior studies examining in-hospital mortality following a wide range of surgical procedures and medical conditions have attributed increased co-morbid burden, age, occurrence of complications, and certain hospital level characteristics such as hospital procedural volumes and teaching status to be significantly correlated with mortality [20-23]. However, complications such as infectious events occurred in 8.1% of patients. We could not specifically examine the risks of the individual infectious events since the rates were low and the multivariable regression models did not converge. We found that occurrence of an infectious event was associated with substantial increases in hospital charges and length of stay in hospital.

The current study results are subject to several limitations and our conclusions should be interpreted keeping these in view. As mentioned earlier, the current study is a retrospective analysis of a large hospital based discharge dataset. The study examines only an association and not a cause and effect relationship between the patient/hospital level variables and occurrence of adverse effect of medical care. The retrospective nature of the study design precludes us from deriving definitive cause and effect relationship. We examined co-morbid burden and used this as a predictor variable in our models. While the presence of a co-morbid condition was identified, the actual severity of the condition was not known. This could certainly influence the outcome and was not accounted for in the regression model. Adverse effects of medical care were identified by using a comprehensive set of injury codes. Even though the validity of the NIS databases have been assessed and found to be valid to conduct health services research we should not discount the possibility of coding biases effecting our study results. Even though the NIS database has been validated for coding errors, we should not discount the possibility of unintended coding biases which are likely to occur when compiling huge volumes of data. Finally, we used ICD-9-CM procedure codes to identify the surgical procedures undergone by patients. Typically CPT codes are used by surgeons and hospitals to code procedures. The NIS database does not provide information on CPT codes. Despite the several limitations identified, our study results are still useful for clinicians, health policy makers, and patients. Our study results are generalizable as our estimates are nationally representative. Our study results reflect the practice patterns and hospitalization outcomes across the country and could serve as benchmarks for future well designed prospective controlled studies to examine risk factors associated with adverse effects of medical care for a wide range of surgical procedures.

CONCLUSION

Orthognathic surgery is an essential part of treatment for patients with cleft lip/palate. This treatment is beneficial for patient esthetics, function, and psychosocial wellbeing and in many cases it is the best option for correcting skeletal discrepancies in patients with cleft lip/palate. This study provides oral surgeons, orthodontists, and patients and their families with additional information about the frequency of adverse effects of surgery, infection, and treatment outcomes. This study is a national representation of these areas of interest and can be used to design future prospective controlled studies to further examine risk factors for these surgical procedures. More importantly, if provides patients with a national representation of surgical outcomes and can help them to make informed decisions prior to undergoing orthognathic surgery. The goal of this study is to provide information that will help improve treatment outcomes for patients with cleft lip/palate.

REFERENCES

1. AAOMS. Link is www.aaoms.org/docs/practice_mgmt/ortho_criteria.pdf. Date of access is 11/21/2013.
2. AAOMS Parameters of Care: Clinical Practice Guidelines for Oral and Maxillofacial Surgery (AAOMS ParCare '12).
3. Parbatani R, Williams AC, Ireland AJ, Sandy JR. The Process of Orthognathic care in an NHS region. Ann R Coll Surg Engl. 2010 January; 92(1): 34–39.
4. Proffit WR, Jackson TH, Turvey TA. Changes in the pattern of patients receiving surgical-orthodontic treatment. Am J Orthod Dentofacial Orthop. 2013 Jun; 143(6):793-8.
5. Boeck EM, Lunardi N, Pinto Ados DS, Pizzol KE, Boeck Neto RJ. Occurrence of skeletal malocclusions in Brazilian patients with dentofacial deformities. Braz Dent J. 2011; 22:340–34.
6. Gerzanic L, Jagsch R, Watzke IM. Psychologic implications of orthognathic surgery in patients with skeletal Class II or Class Ill malocclusion. Int J Adult Orthod Orthognath Surg. 2002;17:75–81
7. Severt TR, Proffit WR. The prevalence of facial asymmetry in the dentofacial deformities population at the University of North Carolina. Int J Adult Orthod Orthognath Surg. 1997; 12:171–176.
8. Silva AC, O'Ryan F, Poor DB (September 2006). "Postoperative nausea and vomiting (PONV) after orthognathic surgery: a retrospective study and literature review". J. Oral Maxillofac. Surg. 64 (9): 1385–97. doi:10.1016/j.joms.2006.05.024. PMID 16916674.
9. Kriwalsky MS, Maurer P, Veras RB, Eckert AW, Schubert J. Risk factors for a bad split during sagittal split osteotomy. Br J Oral Maxillofac Surg. 2008 Apr; 46(3):177-9.
10. Altman JI, Oeltjen JC. Nasal deformities associated with orthognathic surgery: analysis, prevention, and correction. J Craniofac Surg. 2007 Jul; 18(4):734-9.
11. Panula K, Finne K, Oikarinen K (October 2001). "Incidence of complications and problems related to orthognathic surgery: a review of 655 patients". J. Oral Maxillofac. Surg. 59 (10): 1128–36; discussion 1137. PMID 11573165.
12. HCUP Nationwide Inpatient Sample (NIDS). Healthcare Cost and Utilization Project (HCUP). 2012-2014. Agency for Healthcare Research and Quality, Rockville, MD. WWW link is http://www.hcup-us.ahrq.gov/nisoverview.jsp. . Date of access is 10/21/2018.
13. Allareddy V, Ackerman MB, Venugopalan SR, Yadav S, Nanda VS, Nanda R. Longitudinal trends in discharge patterns of orthognathic surgeries: is there a regionalization of procedures in teaching hospitals? Oral Surg Oral Med Oral Pathol Oral Radiol. 2012 Dec 17. doi:pii: S2212-4403(12)01516-7. 10.1016/j.oooo.2012.09.003. [Epub ahead of print]
14. Venugoplan SR, Nanda V, Turkistani K, Desai S, Allareddy V. Discharge patterns of orthognathic surgeries in the United States. Journal of Oral and Maxillofacial Surgery. 2012 Jan; 70(1):e77-86.
15. L.T. Kohn, J.M. Corrigan, M. Donaldson. To Err is Human: Building a Safer Health System. National Academies Press, Washington, DC (2000)

16. Centers for Medicare & Medicaid Services Office of Public Affairs Press Release: Eliminating Serious, Preventable, and Costly Medical Errors—Never Events (Accessed October 10, 2011) Available at: http://www.cms.hhs.gov/apps/media/press/release.asp?
17. C. Zhan, M.R. Miller. Excess length of stay, charges, and mortality attributable to medical injuries during hospitalization. JAMA, 290 (2003), pp. 1868–1874.
18. Panula K, Finne K, Oikarinen K. Incidence of complications and problems related to orthognathic surgery: a review of 655 patients. J. Oral Maxillofac. Surg. 2001 Oct;59 (10): 1128–36; discussion 1137.
19. Van de Perre JP, Stoelinga PJ, Blijdorp PA, Brouns JJ, Hoppenreijs TJ. Perioperative morbidity in maxillofacial orthopaedic surgery: a retrospective study. J Craniomaxillofac Surg. 1996 Oct;24(5):263-70.
20. Allareddy V, Allareddy V, Konety BR. Specificity of procedure volume and in-hospital mortality association. Ann Surg. 2007 Jul;246(1):135-9.
21. Allareddy V, Ward MM, Allareddy V, Konety BR. Effect of meeting Leapfrog volume thresholds on complication rates following complex surgical procedures. Ann Surg. 2010 Feb;251(2):377-83.
22. Capobianco DM, Batilana A, Gandhi M, Shah J, Ferreira R, Carvalho E, Rivero TS, Pietrobon R, Atallah AN, Fernandes do Prado G. Surgical treatment of sleep apnea: Association between surgeon/hospital volume with outcomes. Laryngoscope. 2013 May 27. [Epub ahead of print]
23. Finks JF, Osborne NH, Birkmeyer JD. Trends in hospital volume and operative mortality for high-risk surgery.N Engl J Med. 2011 Jun 2;364(22):2128-37.
24. Allareddy, V. (2014). "Prevalence and impact of complications on hospitalization outcomes following surgical repair for craniosynostosis." J Oral Maxillofac Surg **72**(12): 2522-2530.
25. Allareddy, V. (2015). "Orthognathic Surgeries in Patients With Congenital Craniofacial Anomalies: Profile and Hospitalization Outcomes." Cleft Palate Craniofac J **52**(6): 698-705.
26. Chang, C. S., C. G. Wallace, Y. C. Hsiao, T. C. Lu, S. H. Chen, F. C. Chan, P. K. Chen, J. P. Chen, C. J. Chang and M. S. Noordhoff (2017). "Patient and parent reported outcome measures in cleft lip and palate patients before and after secondary alveolar bone grafting." Medicine (Baltimore) **96**(52): e9541.
27. Forrest, C. R. and R. A. Hopper (2013). "Craniofacial syndromes and surgery." Plast Reconstr Surg **131**(1): 86e-109e.
28. Kim, S. J., M. R. Kim, S. W. Shin, Y. S. Chun and E. J. Kim (2009). "Evaluation on the psychosocial status of orthognathic surgery patients." Oral Surg Oral Med Oral Pathol Oral Radiol Endod **108**(6): 828-832.
29. Lee, M. K., S. L. Yen and V. Allareddy (2018). "Hospitalization Outcomes of Cleft Lip Repair in Neonates Across the United States." Cleft Palate Craniofac J **55**(4): 528-535.
30. Ligh, C. A., J. P. Fox, J. Swanson, J. W. Yu and J. A. Taylor (2016). "Not All Clefts Are Created Equal: Patterns of Hospital-Based Care Use among Children with Cleft Lip and Palate within 4 Years of Initial Surgery." Plast Reconstr Surg **137**(6): 990e-998e.

31. Moran, I., S. Virdee, I. Sharp and J. Sulh (2018). "Postoperative Complications Following LeFort 1 Maxillary Advancement Surgery in Cleft Palate Patients: A 5-Year Retrospective Study." Cleft Palate Craniofac J **55**(2): 231-237.
32. Murphy, C., G. Kearns, D. Sleeman, M. Cronin and P. F. Allen (2011). "The clinical relevance of orthognathic surgery on quality of life." Int J Oral Maxillofac Surg **40**(9): 926-930.
33. Shaye, D. (2014). "Update on outcomes research for cleft lip and palate." Curr Opin Otolaryngol Head Neck Surg **22**(4): 255-259.
34. Zins, J. E., C. M. Morrison, A. M. Gonzalez, G. D. Altus and J. Bena (2008). "Follow-up: orthognathic surgery. Is there a future? A national survey." Plast Reconstr Surg **122**(2): 555-562.
35. Nahai, Farzad R. et al. “The Management of Cleft Lip and Palate: Pathways for Treatment and Longitudinal Assessment” *Seminars in Plastic Surgery* vol. 19,4 (2005): 275–285.
36. Mulliken, John B. “Repair of bilateral cleft lip and its variants” *Indian journal of plastic surgery : official publication of the Association of Plastic Surgeons of India* vol. 42 Suppl,Suppl (2009): S79-90.
37. Orthognathic Surgical Outcomes in Patients With and Without Craniofacial Anomalies Metalwala, Zohra et al. Journal of Oral and Maxillofacial Surgery , Volume 76 , Issue 2 , 436.e1 - 436.e8
38. Boyne PJ, Sands NR. Combined orthodontic-surgical management of residual palato-alvelar cleft defects. Am J Orthod. 1976 Jul;70(1):20-37.
39. Millard DR Jr, Latham RA. Improved primary surgical and dental treatment of clefts. Plast Reconstr Surg. 1990 Nov;86(5):856-71.
40. Millard DR, Latham R, Huifen X, Spiro S, Morovic C. Clieft lip and palate treated by presurgical orthopedics, gingivoperiosteoplasty, lip adhesion (POPLA) compared with previous lip adhesion method: a preliminary study of serial dental casts. Plast Reconstr Surg. 1999 May;103(6):1630-44.
41. Maull DJ, Grayson BH, Cutting CB, Brecht LL, Brookstein FL, Khorrambadi D, Webb JA, HUrwitz DJ. Long-term effects of nasoalveolar molding on three-dimensional nasal shape in unilateral clefts. Cleft Palate Craniofac J. 1999 Sep;36(5):391-7.
42. Singer E, Daskalogiannakis J, Russell KA, Mercado AM, Hathaway RR, Stoutland A, Long RE Jr, Fessler J, Semb G, Shaw WC. Burden of Care of Various Infant Orthopedic Protocols for Improvement of Nasolabial Esthetics in Patients With CUCLP. Cleft Palate Craniofac J. 2018 Oct;55(9):1236-1243. doi:10.1177/1055665618766978. Epub 2018 Apr 6. PubMed PMID: 29624437
43. “Correction of jaw deformities in patients with cleft lip and palate” *Proceedings (Baylor University. Medical Center)* vol. 15,3 (2002): 250-4.
44. "Clinical Classifications Software (CCS) for ICD-9-CM" *Agency for Healthcare Research and Quality. Clinical Classification Software Documentation.* https://www.hcup-us.ahrq.gov/toolssoftware/ccs/ccs.jsp. Accessed 27 December 2018.
45. "Consumer Price Index Inflation Rate Calculator for Hospital Inpatient Care." *BLS - Bureau of Labor Statistics.* http://www.bls.gov/data/inflation_calculator.htm. Accessed 1 April 2018.

46. "International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM)." *Centers for Disease Control and Prevention.* www.cdc.gov/nchs/icd/icd9cm.htm#ftp. Accessed 6 March 2014.
47. Southard, Thomas E., et al. *Orthodontics in the Vertical Dimension: a Case-Based Review*. Wiley Blackwell, 2015.