The Role of Prognostic Factors in Perioperative Adverse Events and Complications in Children with Cleft Palate Repair

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Abstract

Aim: Cleft lip and palate (CLP) deformity is the most common type of craniofacial malformation and is usually corrected surgically in infancy. Anesthetic management of children undergoing CLP repair has many challenges. In this study, it was aimed to evaluate the effect of prognostic factors on perioperative complications in children with cleft palate (CP) repair.

Methods: In this study, pediatric cases who underwent cleft palate surgery in a tertiary care hospital between 2015 and 2020 were analyzed retrospectively. The primary outcome measure was perioperative adverse outcomes rate.

Results: The incidence of all perioperative adverse events including airway, and respiratory complications, ICU admission, blood transfusion and re-operation requirement was determined as 40.7% (n=88) and the incidence of respiratory adverse events was found as 28.7% (n=62). Moreover, low body weight (OR 0.69, 95% CI 1.18-1.78, p<0.001), comorbidity, concomitant presence of syndrome (OR 7.19, 95% CI 2.02-25.60, p<0.001) and cleft lip (OR 2.73, 95% CI 1.10–6.73, p=0.030), and complete type of cleft palate (OR 0.33, 95% CI 1.22–7.46, p=0.017) were risk factors for perioperative adverse events.

Conclusions: In this study, a significant relationship was found between underweight, comorbidity, the presence of concomitant syndrome, cleft lip, complete type of cleft palate and the risk of developing perioperative adverse events in children with CP repair.

Keywords: *Cleft palate, cleft lip, difficult airway, perioperative complications, underweight*

1. Introduction

Craniofacial clefts are deformations of the face and skull as a result of development and/or fusion defects in bone and/or soft tissues along linear anatomical planes[1]. Oral clefts are the most common craniofacial malformations among all congenital anomalies, with three basic types: cleft lip (CL) alone, cleft palate (CP) alone, and cleft lift with cleft palate (CLP)[2]. Although the exact incidence of oral cleft is not known, it is estimated to occur at a rate of 14.5 per 10,000 live births[3]. Treatment for CP is surgical repair of the deformity under general anesthesia when the child reaches a minimum age of 10-12 months. Anesthesia management of these children presents challenges in many aspects. Conditions such as airway problems, accompanying syndromes and musculoskeletal, cardiovascular and central nervous system abnormalities, malnutrition and growth retardation contribute to anesthesia-related morbidity and mortality. Furthermore, recurrent respiratory infections and reactive airway are common in these children due to continuous aspiration and impairment of the protective properties of the airway[4]. This significantly increases the risk of airway and respiratory complications at all stages of anesthesia practice, including induction, maintenance, and recovery[5]. In addition to the anatomical defect, accompanying structural deformities, such as micrognathia, glossoptosis, and airway obstruction, as in the Pierre Robin sequence, increase the risk of encountering a difficult airway[6]. Moreover, children with CLP with maxillary or mandibular hypoplasia, macroglossia, or poor motor tone are at risk for obstructive sleep apnea, which further complicates anesthesia management[6]. Therefore, CP repair, which constitutes an important part of infant and childhood surgeries, is still associated with increased morbidity and mortality. While there are identified risk factors, more evidence is needed in this area that

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could improve patient outcomes. Thus, this study aimed to investigate the prognostic factors affecting the incidence of perioperative adverse events and postoperative complications in pediatric patients undergoing cleft palate repair, and the primary outcome measure was perioperative adverse outcomes rate.

2. Materials and methods

This study was approved by the Institutional Investigation and Ethics Committee on November 6, 2020, with approval number: 105/16 and conducted at Cukurova University in Turkey.

2.1. Patients

For this retrospective cohort study, two hundred sixteen pediatric patients who underwent primary cleft palate repair by the Department of Plastic, Reconstructive and Aesthetic Surgery at Cukurova University Hospital between January 2015 and October 2020 were recruited. Re-operated patients and patients who were scheduled for palatal fistula repair were not included in the study. The sample size of the study consisted of all pediatric patients who had undergone cleft palate repair surgery within the five-year experience of our tertiary care hospital and met the inclusion criteria of the study. Power analysis was not used in the study.

2.2. Data collection

Electronic medical records, anesthesia records, preoperative evaluation records, nursing records, laboratory findings, and postoperative evaluation records and clinical outcomes were reviewed for all patients. All data were collected, recorded and checked by two different independent research assistants.

2.3. Outcomes

From the preoperative records, the demographic characteristics of the patients (age, gender, weight, height), American Society of Anesthesiologists (ASA) physical status classification, cleft palate classification whether being complete, incomplete or submucous cleft palate, concomitant diseases, syndromes, malformations and chromosomal abnormalities, and preoperative laboratory tests were recorded. From the records during the operation, the fluid, blood and blood product use, the presence of difficult airway, bronchospasm, hypercarbia, hypoxemia, and accidental extubation, and the duration of the operation were recorded. From the postoperative period records, the presence of stridor, rhonchi, hypoxemia, need for reintubation, and intensive care unit (ICU) admission and length of ICU stay, the amount of blood and blood products transfusion, need for reoperation, and length of hospital stay were documented.

Perioperative adverse events were defined as difficult mask ventilation, difficult laryngoscopy and intubation, intraoperative blood transfusion, bronchospasm, hypoxemia, hypercarbia, and accidental extubation, requirement of postoperative reintubation, need for ICU admission, blood transfusion, need for reoperation, postoperative respiratory distress and other complications.

2.4. Statistical analysis

IBM SPSS Statistics Version 25.0 package program was used for statistical analysis of the data. Categorical measurements were summarized as numbers and percentages, and continuous measurements as mean and standard deviation (median and minimum-maximum where necessary). The conformity of the variables to the normal distribution was evaluated using histogram and probability graphs and Kolmogorov-Smirnov/Shapiro-Wilk tests. Pearson Chi-square test and Fisher's exact test were used to compare categorical variables. Student's t-test was used for groups with normal distribution in binary variables, and Man-Whitney U test was used for groups that did not fulfill normal distribution. One-way ANOVA tests were used for groups with normal distribution in multiple variables. Logistic regression analysis was performed to determine variables that were predictors of perioperative adverse outcomes. Statistical significance level was accepted as 0.05 in all tests.

3. Results

Two hundred and seventy-eight patients were evaluated for this study. A total of 62 patients were excluded from the study because 39 patients were scheduled for reoperation and 23 patients had palatal fistula repair. Thus, this study was conducted with two hundred sixteen pediatric patients obtained from a single center's 5-year cleft palate repair experience. The mean age of the children was 621.5±28.0 days. The demographic characteristics and the medical history of the patients were represented in Tables 1 and 2.

14 (6.5%) of the patients had a documented difficult airway. Respiratory complications such as bronchospasm, hypercapnia and hypoxemia were observed in 53 (24.5%) patients in the intraoperative period, while airway and respiratory complications were detected in 27 (12.5%) patients in the postoperative period (Table 3).

The overall rate of perioperative adverse events including difficult airway, intra- and postoperative airway and respiratory complications, intra- and postoperative blood transfusion, post-

Table 1

Patient Characteristics and Length of Hospital Stay

Number of patients	n=216
Age (day)*	621.5±28.0
Gender (M/F)†	115(53.2)/101(46.8)
Weight (kg)*	10.5±2.4
Weight percentile†	
• <25%	122(56.5)
• 25-75%	69(31.9)
• >75%	25(11.5)
ASA physical status†	
• I	178(82.4)
• II	38(17.6)
Type of cleft palate†	
• Complete	95(44.0)
• Incomplete	108(50.0)
• Submucous	13(6.0)
Indication for surgery†	
• Isolated CP	125(57.9)
• CLP	91(42.1)
Length of hospital stay‡	4(2-21)

Abbreviations: ASA, American Society of Anesthesiologists; CP, cleft palate; CLP, cleft lip and palate. *Values are given as mean±standard deviation. †Values are given as n (%). ‡Value is given median (min-max)

Table 2

Preoperative Concomitant Diseases, Anemia and Syndromes

Chromosomal abnormality	3(1.4)
Syndrome	16(7.4)
• Pierre-Robin	4(1.9)
• Others*	12(5.5)
Concomitant diseases	45(20.8)
• Congenital heart disease	24(11.1)
• CNS disease	7(3.2)
• Metabolic disease	3(1.4)
• Others**	11(5.1)
Preoperative anemia	58(26.9)

Abbreviations: CNS, central nervous system. Values are given as n (%). *Including Cat Eye, Dandy Walker, Sotos and Charge syndromes. **Including pulmonary, skeletal and renal abnormalities.

Table 3
Airway and Respiratory Complications

Difficult airway	14(6.5)
• Difficult mask ventilation	2(0.9)
• Difficult intubation	12(5.6)
Prolonged intubation	4(1.9)
Re-intubation	2(0.9)
Intraoperative respiratory complications	53(24.5)
• Bronchospasm	33(15.3)
• Hypercapnia	10(4.6)
• Hypoxemia	2(0.9)
Accidental extubation	8(3.7)
Postoperative respiratory complications	27(12.5)
• Stridor	12(5.6)
• Roncus	12(5.6)
• Hypoxemia	2(0.9)
• Pneumothorax	1(0.5)

Values are given as n (%).

Table 4
Perioperative Adverse Outcomes

Perioperative adverse events*	88(40.7)
Intraoperative blood transfusion	18(8.3)
Postoperative blood transfusion	23(10.6)
Postoperative ICU admission	20(9.3)
Re-operation	45(20.8)

Abbreviations: ICU, intensive care unit. *Including difficult airway, intra- and postoperative airway and respiratory complications, intra- and postoperative blood transfusion, postoperative ICU admission, and re-operation requirement. Values are given as n (%).

operative ICU admission, and re-operation requirement were 40.7% (n=88) (Table 4).

When the occurrence of perioperative adverse events and the prognostic factors of the patient were compared, a significant relationship was found between the ASA II physical status, the presence of complete type cleft palate and concomitant cleft lip, and adverse events (Table 5).

On the other hand, when only perioperative respiratory complications and prognostic factors were compared, a significant correlation was found between low body weight, concomitant syndrome and comorbidity, and respiratory complications (Table 6).

According to the Logistic Regression analysis, it was determined that weight, type of cleft palate, history of cleft lip operation, presence of concomitant syndrome are risk factors for intraoperative adverse respiratory events. According to this: each one kg decrease in body weight increases the risk of intraoperative adverse respiratory events by 1.45 times (OR 0.69, 95% CI 1.18-1.78, p<0.001); type of complete cleft palate increases the risk of intraoperative adverse respiratory events by 3.02 times (OR 0.33, 95% CI 1.22–7.46, p=0.017) compared to incomplete type; the presence of concomitant cleft lip increases the risk of intraoperative adverse respiratory events by 2.73 times (OR 2.73, 95% CI 1.10–6.73, p=0.030); the presence of the syndrome increases the risk of intraoperative adverse respiratory events by 7.19 times (OR 7.19, 95% CI 2.02-25.60, p<0.001) were determined (Table 7).

Furthermore, in the Logistic Regression analysis for the postoperative adverse event, only the length of hospital stay was determined as a risk factor, and it was observed that each 1-day increase in hospital stay increased the risk of postoperative adverse events by 1.6 times (OR 0.06, 95% CI 1.29-1.99, p<0.001) (Table 8).

4. Discussion

In this retrospective cohort study, in which pediatric cases with primary cleft palate repair were analyzed, the incidence of all perioperative adverse events including airway, and respiratory complications, ICU admission, blood transfusion and re-operation requirement was determined as 40.7% (n=88) and the incidence of respiratory adverse events was found as 28.7% (n=62). Moreover, low body weight, comorbidity, concomitant presence of syndrome and cleft lip, and complete type of cleft palate were risk factors for perioperative adverse events.

A difficult airway is more common in children with CLP repair than other surgical pediatric patients7. Developmental defect of the linear anatomical planes in the craniofacial area makes it difficult for mask ventilation and laryngoscopy in certain patients6,7. In addition, the accompanying syndromes or OSA, which are accepted as risk factors for difficult airway, increase this risk even more8. In this study, difficult airway was documented in 14 (6.5%) patients, the majority of whom were difficult intubation (5.6%) and two (0.9%) were unsuccessful intubation. The prevalence of difficult intubation has been reported as 1.3-3.0% in studies examining various types of pediatric surgical patients9,10. As expected, the rate of difficult intubation in children who underwent CLP repair was reported to be 2.4-4.8%, higher than the other pediatric population5,11-13. When the studies are examined individually, it is understood that the rate of difficult airway is proportional to the

Table 5
Relationship Between Perioperative Adverse Events and Prognostic Factors

	Perioperative adverse events		
	Yes (n=88)	No (n=128)	p value
ASA physical status			0.001*
• I	63(71.6)	115(89.8)	
• II	25(28.4)	13(10.2)	
Weight percentile			0.485
• < 50%	67(76.1)	92(71.9)	
• > 50%	21(23.9)	36(28.1)	
Type of cleft palate			0.003*
• Complete	50(56.8)	45(35.2)	
• Incomplete	36(40.9)	72(56.2)	
• Submucous	2(2.3)	11(8.6)	
Concomitant cleft lip			0.001*
• Yes	49(55.7)	42(32.8)	
• No	39(44.3)	86(67.2)	

Abbreviations: ASA, American Society of Anesthesiologists. Values are given as n (%). *These values indicate statistical significance (p<0.05).

Table 6

Relationship Between Perioperative Respiratory Complications and Prognostic Factors

	Perioperative respiratory complications		
	Yes (n=62)	No (n=154)	p value
Weight percentile			0.004*
• < 50%	54(87.0)	105(68.1)	
• > 50%	8(13.0)	49(31.9)	
Type of cleft palate			0.478
• Complete	24(38.7)	71(46.1)	
• Incomplete	35(46.5)	73(47.4)	
• Submucous	3(4.8)	10(6.5)	
Concomitant cleft lip			0.119
• Yes	21(33.9)	70(45.5)	
• No	41(66.1)	84(54.5)	
Concomitant disease			
• Yes	25(40.3)	20(13.0)	0.001*
• No	37(59.7)	134(87.0)	
Concomitant syndrome			
• Yes	11(17.7)	5(3.2)	0.001*
• No	51(82.3)	149(96.8)	

Values are given as n (%). *These values indicate statistical significance (p<0.05).

Table 7

Logistic Regression Analysis of the Association Between Intraoperative Adverse Events and Prognostic Factors

Variable	Coefficient	SE	OR	Adjusted OR (95% CI)	p value
Complete type of cleft palate†	-1.106	0.462	0.331	1.220-7.460	0.017*
Concomitant cleft lip	1.003	0.461	2.727	1.105-6.731	0.030*
Concomitant syndrome	1.973	0.648	7.190	2.020-25.599	0.002*
Weight (kg)	-0.373	0.106	0.689	1.180-1.780	0.001*

Abbreviations: OR, odds ratio; CI, confidence interval.†According to reference category of incomplete type of cleft palate.*These values indicate statistical significance (p<0.05).

Table 8

Logistic Regression Analysis of the Association Between Postoperative Adverse Events and Prognostic Factors

Variable	Coefficient	SE	OR	Adjusted OR (95% CI)	p value
Length of hospital stay (day)	-2.752	0.533	0.064	1.290-1.990	<0.001*

Abbreviations: OR, odds ratio; CI, confidence interval.
*These values indicate statistical significance (p<0.05).

number of concomitant syndromic pediatric patients in the study population. Since the hospital where the current study was conducted was a tertiary care level, complicated patients were included in this study at a higher rate, and the prevalence of difficult airway was found to be higher than expected.

The presence of a reactive airway, other accompanying structural anomalies, and the intersection of the airway and the surgical field are the main reasons that increase the frequency of perioperative respiratory complications in children who have undergone CLP[4-6,8]. In this study, the incidence of all perioperative respiratory complications, including bronchospasm, hypercapnia, hypoxia, laryngeal edema, and pneumothorax, was calculated as 28.7%, and intraoperative bronchospasm was the most common complication (15.3%). In a study of children undergoing CLP repair, it was noted that respiratory complications, most commonly desaturation, were more than twice as common in patients with CP (38.4%) compared to patients with CL alone (15.8%)[5]. In another study, 460 pediatric patients with CP were analyzed and the respiratory complication rate was 8.7%[11]. This rate, which is inconsistent with our results, was interpreted as the majority of the patients were in the 3-8 age group. Feeding problems are common in children with CLP, so they are at high risk of growth failure and developmental delay. Preoperative malnutrition is associated with higher rates of postoperative complications in various type of surgery as well as CLP repair[14,15]. It is well known that there is a significant increase in the incidence of anesthesia and surgical related complications such as airway difficulties, wound healing problems, re-operation requirement, and prolonged hospitalization, especially in infants with less than 10 kg body weight or underweight (less than 50% percentile)[14-16]. Similarly, in this study we obtained that underweight is an independent risk factor for perioperative complications in both univariate analysis and logistic regression model.

CLP is frequently accompanied by additional malformations, including syndromes and various organ system anomalies, which vary geographically and ethnically[6-8]. The most common syndrome accompanying CLP is Pierre-Robin syndrome and the most common organ system malformation is congenital heart disease[6,17,18]. Comparatively, in this study, the most common comorbidity was congenital heart disease and the most common associated syndrome was Pierre-Robin syndrome, and both were identified as independent risk factors for adverse outcomes in the analysis of the data.

It is known that the complete type of cleft palate is associated with difficult laryngoscopy, frequent recurrent infections and fistula formation[19-21]. In the results of the present study, it was determined that the complete type of cleft palate and presence of concomitant cleft lip are associated with increased perioperative adverse outcomes compared to the incomplete type.

The strength of this study is that it consists all cleft palate cases in the 5-year experience of a tertiary reference regional hospital. However, the present study had some limitations such as being a single-center retrospective study, insufficient number of patients to be able to make subgroup analyzes more reliable, and the insufficient level of some data records.

5. Conclusions

According to the results obtained from this study, low body weight, presence of comorbidities, especially congenital heart disease, concomitant syndrome or chromosomal abnormality, complete type of cleft palate and associated cleft lip increase the incidence of perioperative adverse events in pediatric patients who have undergone cleft palate repair surgery. However, further multicenter prospective studies that include more reliable analyzes of subgroups such as malformations, syndromes and chromosomal abnormalities associated with cleft palate are needed to determine the factors that will improve patient outcomes in the anesthesia management of the children with cleft palate repair.

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Statement of ethics

The study was registered at the Cukurova University Institutional Investigation and Ethics Committee on 6 November 2020 with the approval number: 105/16 and conducted at Cukurova University in Turkey following the most recent version of the Declaration of Helsinki.

Conflict of interest statement

The authors declare that they have no financial conflict of interest with regard to the content of this report.

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Author contributions

EEI conducted the methodology, data collection and processing, writing, reviewing and editing processes.
DLT handled the conceptualization, design, supervision, literature review, conduction and writing - original draft preparation. All authors contributed to the final manuscript revisions and approved the final version.

References

1.Tessier P. Anatomical classification facial, cranio-facial and latero-facial clefts. J Maxillofac Surg. 1976; 4(2): 69-92.
https://doi.org/10.1016/s0301-0503(76)80013-6
2.Marazita ML, Mooney MP. Current concepts in the embryology and genetics of cleft lip and cleft palate. Clin Plast Surg. 2004; 31(2): 125-40.
https://doi.org/10.1016/S0094-1298(03)00138-X
3.Mai CT, Cassell CH, Meyer RE, et al. Birth defects data from population-based birth defects surveillance programs in the United States, 2007 to 2011: highlighting orofacial clefts. Birth Defects Res A Clin Mol Teratol. 2014; 100(11): 895-904.
https://doi.org/10.1002/bdra.23329
4.Murat I, Constant I, Maud'huy H. Perioperative anaesthetic morbidity in children: a database of 24,165 anaesthetics over a 30-month period. Paediatr Anaesth. 2004; 14(2): 158-66.
https://doi.org/10.1111/j.1460-9592.2004.01167.x
5.Desalu I, Adeyemo W, Akintimoye M, et al. Airway and respiratory complications in children undergoing cleft lip and palate repair. Ghana Med J. 2010; 44(1): 16-20.
https://doi.org/10.4314/gmj.v44i1.68851
6.Denning S, Ng E, Wong Riff KWY. Anaesthesia for cleft lip and palate surgery. BJA Educ. 2021; 21(10): 384-9.
https://doi.org/10.1016/j.bjae.2021.06.002
7.Nargozian C. The airway in patients with craniofacial abnormalities. Paediatr Anaesth. 2004; 14(1): 53-9.
https://doi.org/10.1046/j.1460-9592.2003.01200.x
8.Milerad J, Larson O, Hagberg C, et al. Associated malformations in infants with cleft lip and palate: a prospective, population-based study. Pediatrics. 1997; 100(2 Pt 1): 180-6.
https://doi.org/10.1542/peds.100.2.180
9.Heinrich S, Birkholz T, Ihmsen H, et al. Incidence and predictors of difficult laryngoscopy in 11,219 pediatric anesthesia procedures. Paediatr Anaesth. 2012; 22(8): 729-36.
https://doi.org/10.1111/j.1460-9592.2012.03813.x
10.Mirghassemi A, Soltani AE, Abtahi M. Evaluation of laryngoscopic views and related influencing factors in a pediatric population. Paediatr Anaesth. 2011; 21(6): 663-7.
https://doi.org/10.1111/j.1460-9592.2011.03555.x
11.Kulkarni KR, Patil MR, Shirke AM, et al. Perioperative respiratory complications in cleft lip and palate repairs: An audit of 1000 cases under 'Smile Train Project'. Indian J Anaesth. 2013; 57(6): 562-8.
https://doi.org/10.4103/0019-5049.123328
12.Gunawardana RH. Difficult laryngoscopy in cleft lip and palate surgery. Br J Anaesth. 1996; 76(6): 757-9.
https://doi.org/10.1093/bja/76.6.757
13.Xue FS, Zhang GH, Li P, et al. The clinical observation of difficult laryngoscopy and difficult intubation in infants with cleft lip and palate. Paediatr Anaesth. 2006; 16(3): 283-9.
https://doi.org/10.1111/j.1460-9592.2005.01762.x
14.Tay CL, Tan GM, Ng SB. Critical incidents in paediatric anaesthesia: an audit of 10 000 anaesthetics in Singapore. Paediatr Anaesth. 2001; 11(6): 711-8.
https://doi.org/10.1046/j.1460-9592.2001.00767.x
15.Escher PJ, Zavala H, Lee D, et al. Malnutrition as a risk factor in cleft lip and palate surgery. Laryngoscope. 2021; 131(6): E2060-5.
https://doi.org/10.1002/lary.29209
16.Argent AC, Balachandran R, Vaidyanathan B, et al. Management of undernutrition and failure to thrive in children with congenital heart disease in low- and middle-income countries. Cardiol Young. 2017; 27(S6): S22-S30.
https://doi.org/10.1017/S104795111700258X
17.Fraser GR, Calnan JS. Cleft lip and palate: seasonal incidence, birth weight, birth rank, sex, site, associated malformations and parental age. A statistical survey. Arch Dis Child. 1961; 36(188): 420-3.
https://doi.org/10.1136/adc.36.188.420
18.Kantar RS, Cammarata MJ, Rifkin WJ, et al. Outpatient versus inpatient primary cleft lip and palate surgery: analysis of early complications. Plast Reconstr Surg. 2018; 141(5): 697e-706e.
https://doi.org/10.1097/PRS.0000000000004293
19.Schultz RC. Management and timing of cleft palate fistula repair. Plast Reconstr Surg. 1986; 78(6): 739-47.
https://doi.org/10.1097/00006534-198678060-00004
20.Nagase Y, Natsume N, Kato T, et al. Epidemiological analysis of cleft lip and/or palate by cleft pattern. J Maxillofac Oral Surg. 2010; 9(4): 389-95.
https://doi.org/10.1007/s12663-010-0132-6
21.Suzuki A, Mukai Y, Ohishi M, et al. Relationship between cleft severity and dentocraniofacial morphology in Japanese subjects with isolated cleft palate and complete unilateral cleft lip and palate. Cleft Palate Craniofac J. 1993; 30(2): 175-81.
https://doi.org/10.1597/1545-1569_1993_030_0175_rbcsad_2.3.co_2