

Treatment of 4-5 year old patients with Cleft Lip and Cleft palate in Tawanchai Center: Prevalence and Type of Associated Malformations

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Background: Patients with cleft lip/palate may have other associated malformations but the reported prevalence and type of associated malformations varied between different studies.

Objective: To report the prevalence and the type of associated malformations in Northeastern Thai patients with cleft lip/palate.

Material and Method: A retrospective study of 123 cleft lip/palate patients aged 4-5 years was carried out at the Tawanchai Cleft Center, Khon Kaen University during the period from October to December 2011. Data were collected by reviewing the patient's medical records.

Results: Seventeen (14%) of the 123 patients had associated malformations. Four (21%) of the 19 patients with cleft palate, eleven (15%) of the 74 patients with clefts lip and palate, and two (7%) of the 30 patients with cleft lip had associated malformations. The organ systems affected by associated malformations were cardiovascular system (41%), craniofacial anomaly (23%), skeletal system (12%), urogenital system (12%) and central nervous system (12%). Atrial septal defect and tetralogy of Fallot were most common associated cardiovascular malformation found.

Conclusion: The high prevalence of associated malformations found in patients with cleft lip/palate emphasizes the need for a thorough screening of associated malformations and congenital heart disease of all cleft lip/palate patients.

Keywords: Cleft lip, Cleft palate, Associated malformations, Congenital heart disease

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Cleft lip (CL) and cleft palate (CP) are the most frequent apparent congenital malformations of the head and neck^(1,2). The worldwide incidence varies between 0.8 and 2.5 cases per 1,000 live births^(1,3-5) and is highest among American Indian and Asian children⁽⁵⁾. Clefts lip and palate have complex etiologies with environmental and genetic risk factors obtained in different countries and regions⁽⁶⁾. Clefts of lip and palate can occur as an isolated problem or may be associated with a syndrome. Clefts of lip and palate are often associated with other congenital malformations⁽⁷⁻¹⁴⁾.

However, there are considerable differences on the reported prevalence and type of associated

congenital malformations observed among different studies around the world⁽⁷⁻¹⁴⁾. The reported prevalence of associated other congenital malformations varies from 1.5% to 63.4%⁽⁷⁻¹⁴⁾. Moreover, there are no agreements of the previous reports on which organ system is the most often affected by associated congenital malformations. Studies from Sweden, Pakistan, and Jordan⁽⁸⁻¹¹⁾ found congenital heart disease was the most common associated congenital malformation whereas Shprintzen et al from USA⁽¹²⁾ documented malformations in the craniofacial area to be the most common associated congenital malformation. In addition, Lilius et al from Finland⁽¹³⁾ documented that the most common associated malformations were the congenital malformation of the extremities while Stoll et al from France⁽¹⁴⁾ found a central nervous system anomaly to be the most common. Thus, there is no consensus on the reported prevalence

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and type of associated malformations in cleft lip and palate patients⁽⁷⁻¹⁴⁾, and there is no previous report from Thailand. Therefore, the authors reported the prevalence and the type of associated congenital malformations in Northeastern Thai patients with cleft lip and palate who were followed-up by the multidisciplinary teams at the Tawanchai cleft center until 4-5 years of age.

Material and Method

The present study was approved by the Human Research Ethics Committee, Khon Kaen University (KKU), with the approval number of HE541281. During October to December 2011, there were 123 cleft lip and palate patients who had the continuous multidisciplinary treatment and followed-up care until 4-5 years of age at the Tawanchai cleft Center, Srinagarind Hospital, Faculty of Medicine, KKU^(1,15).

The methodology of the continuous multidisciplinary care had been reported elsewhere^(1,15). In brief, of the 123 patients, 120 (98%) cases had operations at Tawanchai Center⁽¹⁾ and 38 (31%) cases came to receive treatment at the age of less than 1 month. The average of number of follow-up visits of the study patients was 18.4 (range, 10-220) visits⁽¹⁵⁾. However, the present report was focusing on the prevalence and type of associated malformations in cleft lip and palate patients. The clinical data were retrospectively collected including: patient's sex, age, type of cleft and type of an associated malformation. All children underwent a thorough clinical examination by a pediatrician. The children, who were considered to have congenital heart disease, were examined in detail by pediatric cardiologists. This was supplemented with an echocardiography. An abnormality was recorded as an associated malformation if it required follow-up or intervention. Dental anomaly was excluded because it was closely related to the cleft and may not be regarded as a separate malformation. The associated malformation was classified according to the organ system primarily affected. A single associated malformation was considered to be present if only one organ system was affected. A multiple associated malformation was considered to be present if two or more than two organ systems were affected.

Statistical analysis

Categorical data were compared using either the Chi-square test or the Fisher's exact test when appropriate. A *p*-value of less than 0.05 was considered

statistically significant.

Results

There were 123 patients in this study group with 70 (57%) boys and 53 (43%) girls. Of these patients, 74 (60%) patients had both cleft lip and palate (CLCP), 30 (24%) patients had isolated cleft lip (CL), and 19 (16%) patients had isolated cleft palate (CP). Twenty patients were originally from Khon Kaen province.

Prevalence of associated malformations

Seventeen (14%) of the 123 patients had associated malformations which required follow-up and/or treatment. In the group with associated malformations, there were 8 (47%) boys compared to 9 (53%) girls, while there were 62 (58%) boys and 44 (42%) girls in the group without any associated malformations (*p* = 0.377).

Eleven (15%) of the 74 patients with CLCP, two (7%) of the 30 patients with CL, and four (21%) of the 19 patients with CP had associated malformations. Although CP had a slight higher prevalence of associated malformations than CLCP and CL, there was no statistically significant difference between these groups (Table 1).

Type of associated malformations

The organ systems affected by associated malformations including cardiovascular system, craniofacial anomaly, skeletal system, urogenital system and central nervous system are shown in Table 2. The most common organ system involved was the cardiovascular system which was found in 7 (41%) patients. Craniofacial anomalies were found in 4 (23%) patients and one of these patients had fronto-ethmoidal meningoencephalocele. Another one patient with craniofacial anomaly had ptosis of the eyes. Malformation of the skeletal system was found in 2 (12%) patients. Of the 2 patients, syndactyly of hand was found in a patient and club foot was found in the other patient. Urogenital malformations were found in 2 (12%) male patients. Hypospadias was found in both patients and one of the two patients also had undescended testes. Malformation of the central nervous system was found in 2 (12%) patients.

Congenital heart disease (CHD)

CHD was found in 5.7 % of the study patients and was present in 7 (41%) of the 17 patients with associated malformations (Table 2). The most common single associated malformation in this study was

Table 1. Characteristics of patients with cleft lip/palate and associated malformations who had received the continuous multidisciplinary treatment and followed-up care at the Tawanchai cleft center in Northeastern Thailand, 2011

Characteristics (number of patients)	Associated malformations		<i>p</i> -value*
	With (17)	Without (106)	
Sex			
Boy (70)	8	62	0.377 ⁺
Girl (53)	9	44	
Cleft lip and palate (74)	11	63	0.680 ⁺
Cleft lip (30)	2	28	0.238 ⁺⁺
Cleft palate (19)	4	15	0.298 ⁺⁺

* A *p*-value of less than 0.05 was considered statistically significant. ⁺ using the Chi-square test; ⁺⁺ using the fisher's exact test

Table 2. Distribution of associated malformations by affected organ systems in different type of cleft patients at the Tawanchai Cleft Center in Northeastern Thailand, 2011

Associated malformations (number of patients)	Type of clefts			<i>p</i> -value*
	CLCP (11)	CL (2)	CP (4)	
Congenital heart disease (7)	5	0	2	0.606 ⁺
Craniofacial anomaly (4)	2	1	1	0.723 ⁺
Skeletal anomaly (2)	2	0	0	>0.999 ⁺
Urogenital system (2)	1	0	1	0.596 ⁺
Central nervous system (2)	1	1	0	0.272 ⁺

CLCP indicates cleft lip and palate; CL = cleft lip; CP = cleft palate.

* A *p*-value of less than 0.05 was considered statistically significant.

⁺ using the Fisher's exact test

Table 3. Distribution of associated malformations by affected organ systems and in different number of organ system involved

Associated malformations* (number of patients)	Single malformation (8)	Multiple malformation (9)	<i>p</i> -value ⁺
Congenital heart disease (7)	4	3	0.637 ⁺⁺
Craniofacial anomaly (4)	3	1	0.294 ⁺⁺
Skeletal anomaly (2)	0	2	0.471 ⁺⁺
Urogenital system (2)	1	1	>0.999 ⁺⁺
Central nervous system (2)	0	2	0.471 ⁺⁺

* Some of patients with associated malformations had recognized syndromes

⁺ A *p*-value of less than 0.05 was considered statistically significant

⁺⁺ Using the Fisher's exact test

congenital heart disease. Isolated secundum type of atrial septal defect (ASD secundum) (2 patients) and tetralogy of Fallot (2 patients) were most common followed by patent ductus arteriosus (PDA) (1 patient), ventricular septal defect (1 patient) and ASD secundum

with PDA (1 patient).

Discussion

The present study has documented the prevalence and type of associated malformations in

children with clefts of lip and palate treated in KKU during October to December 2011. The prevalence of associated malformations was 14% of the 123 patients which was similar to the 14% found in a previous retrospective study from Jordan⁽¹⁰⁾. The most common associated malformation in this study was congenital heart disease which occurred in 41% of the patients with associated malformations. Atrial septal defect and tetralogy of Fallot were the most frequent congenital heart diseases found. This finding was similar to the previous reports from Sweden, Pakistan, Jordan and East China⁽⁸⁻¹¹⁾. The next most common associated malformations were craniofacial anomaly, skeletal system, urogenital system and central nervous system. The prevalence rates of associated malformations found in patients with cleft lip and palate were not evenly distributed among the 3 cleft groups (CLCP, CL, and CP) in the present study. Although, in the present study, the rate of associated malformations was 21% in patient with CP, 15% in patients with CLCP and 7% in patients with CL, there was no significant difference among the three groups. This finding accorded the previous observation that patients with CP were more likely to have associated malformations than those with CLCP and CL⁽⁹⁻¹¹⁾. However, the present study did not support the observation that the more severe cleft involvement (like cleft lip and palate) was associated with a higher frequency of associated malformation^(8,12).

According to previous studies on associated malformations in patients with cleft lip/palate, there were variations of the prevalence rates of associated malformations⁽⁷⁻¹⁴⁾. The hospital-based studies tended to report higher prevalence rates as compared to the population-based studies. The hospital-based data could also have variations of the prevalence rates of associated malformations according to the type of expertise of the hospitals or centers. The different in methodologies of gathering data from birth, from different ages or from varying races or no consensus of definitions/classifications, which themselves had different prevalence and type of associated malformations in patients with cleft lip and palate⁽⁷⁻¹⁴⁾. In different countries, there was also a wide variation on the common type associated malformations in patients with cleft lip and palate⁽⁷⁻¹⁴⁾. In the present study, the common associated malformations were cardiovascular system (41%), craniofacial anomaly (23%), skeletal system (12%), urogenital system (12%) and central nervous system (12%).

Among the associated malformations, congenital heart disease was the common associated

malformation and was found in 7 patients. This represents a prevalence rate of approximately 5.7% of the study group. The reported prevalence of congenital heart disease in Thai population is 0.44%⁽¹⁶⁾. Therefore the risk of congenital heart disease in cleft patients is approximately 13 times that of the general Thai population which is comparable to previous reports from France, Sweden and Pakistan of 5-23 times of the general population risks^(8-9,14).

Study limitation

The present study is hospital based and the prevalence rate reported cannot be generalized to the whole Thai population. This study concentrated only cleft lip and palate patients attending to the Tawanchai cleft Center, Faculty of Medicine, Khon Kaen University who were treated and followed-up until 4-5 years of age. Although the clinical data were retrospectively collected, all study patients underwent a thorough clinical examination by pediatricians. The patients, who were considered to have congenital heart disease, were examined in detail by pediatric cardiologists with the utilization of an echocardiography. However, the present study is conducted on the largest cleft lip and palate center in Northeastern Thailand. Moreover, the clinical information on each cleft lip/palate patient was reviewed by the plastic surgeon and the pediatrician to ensure the accurate definition and classification. Therefore, the authors have confidence that the results of this study have certain value for clinicians and health care providers.

Conclusion

The high prevalence of associated malformations found in patients with cleft lip and palate emphasizes the need for a thorough screening of associated malformations and congenital heart disease of all cleft lip and palate patients.

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Potential conflicts of interest

None.

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การรักษาผู้ป่วยปากแหว่งเพดานโหว่ในช่วงอายุ 4-5 ปีของศูนย์ตะวันฉาย: ความชุกและชนิดของรูปร่างที่พบร่วม

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ภูมิหลัง: ความชุกและชนิดของรูปร่างที่พบร่วมในผู้ป่วยปากแหว่งเพดานโหว่จากรายงานต่างๆ มีความแตกต่างกันมาก

วัตถุประสงค์: เพื่อศึกษาความชุกและชนิดของรูปร่างที่พบร่วมในผู้ป่วยปากแหว่งเพดานโหว่ที่ภาคตะวันออกเฉียงเหนือ

วัสดุและวิธีการ: ศึกษาเวชระเบียนผู้ป่วยปากแหว่งเพดานโหว่ ที่มารับการรักษาที่ศูนย์ตะวันฉายอย่างต่อเนื่องจนมีอายุ 4-5 ปี ในช่วงตุลาคมถึงธันวาคม พ.ศ. 2554

ผลการศึกษา: ผู้ป่วยปากแหว่งเพดานโหว่จำนวน 123 ราย มีรูปร่างที่พบร่วมจำนวน 17 ราย (ร้อยละ 14) รูปร่างที่พบได้แก่ ระบบหัวใจและหลอดเลือด (ร้อยละ 41) ความพิการที่ศีรษะและใบหน้า (ร้อยละ 23) ระบบโครงกระดูก (ร้อยละ 12) ระบบทางเดินปัสสาวะและอวัยวะสืบพันธุ์ (ร้อยละ 12) ระบบประสาทส่วนกลาง (ร้อยละ 12) โรคหัวใจพิการแต่กำเนิดที่พบบ่อยได้แก่ผนังหัวใจห้องบนรั่วและ tetralogy of Fallot

สรุป: ความชุกของรูปร่างที่พบร่วมในผู้ป่วยปากแหว่งเพดานโหว่มีอัตราที่สูง ควรมีการคัดกรองตรวจหารูปร่างที่พบร่วมรวมทั้งโรคหัวใจพิการแต่กำเนิดในผู้ป่วยปากแหว่งเพดานโหว่อย่างละเอียด
