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The relationship between external bony defects and widened lateral interorbital distance in frontoethmoidal encephalomeningocele

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ABSTRACT

Purpose: The aim of this study was to identify the prevalence of the abnormal lateral interorbital distance (LIOD), microphthalmia or anophthalmia and incidence of hydrocephalus in frontoethmoidal encephalomeningocele (FEEM), and to identify the correlation between the external bony defects and a widened lateral orbital wall.

Materials and methods: FEEM patients who were treated in the Faculty of Medicine, Chiang Mai University between January 1, 2006, and December 31, 2016, were retrospectively reviewed from the medical records. We included the patients who had undergone head computed tomography (CT) of the facial bones. Exclusion criteria were any patients who had undergone prior facial surgery or had maxillofacial bone trauma before they underwent a CT scan, craniofacial disease such as facial clefts, frontonasal dysplasia, craniosynostosis, and inter-frontal encephalocele. Measurements were taken from the CT images to establish the diameter of the external bony defect, medial interorbital distance and lateral interorbital distance. The relationships between the external bony defect and widened LIOD were analyzed. Patients were divided into two groups: those with normal LIOD and those with wide LIOD.

Results: A total of 94 FEEM patients were evaluated. Thirteen patients (13.83%) had a wider than normal LIOD. The incidence of microphthalmia or anophthalmia was 9.57% and hydrocephalus was 45.74%. From a univariable model, there were no statistically significant differences in terms of patient characteristics between the LIOD groups, except for sex. The proportion of wide LIOD was higher in male patients (male vs female; 20.34% vs 2.86%, $p = 0.027$). The proportion between the external bony defect and the LIOD (EL ratio) associated with a wide LIOD was shown in a cutoff point of 23% (AuROC = 73.27%, 95% CI = 59.87%–86.66%). The multivariable analysis indicated factors associated with abnormal LIOD were an EL ratio of 23% (adjusted RR = 1.98, 95% CI = 1.58–2.51) and male sex (adjusted RR = 6.85, 95% CI = 2.00–23.55).

Conclusion: There is an association between the EL ratio and widening of the LIOD. An EL ratio greater than 23% could be used to moderately predict a wide LIOD. A large external bony defect may be associated with lateral displacement of the orbit causing true hypertelorism. Therefore, orbital translocation must be considered in patients with a wide LIOD.

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1. Introduction

Frontoethmoidal encephalomeningocele (FEEM) is a congenital anomaly. This condition is a herniation of the brain and meninges through a skull defect, known as the foramen cecum, located at the junction between the frontal and ethmoid bones (Suwanwela and

Suwanwela, 1972). This defect causes an encephalocele to emerge from the intracranium into the extracranium. Patients usually present with a mass or masses in the perinasal, forehead or medial canthal area, the masses varying in size. A high incidence of FEEM has been found in Southeast Asia, especially in Malaysia, Thailand, and Myanmar. The incidence rate is in 1:5,000–6,000 live births (Chowchuen et al., 2011). In Thailand, most FEEM patients come from the lower northern and northeast regions (Rojvachiranon, 2006). Clinically, the mass(es) in the perinasal or medial orbital areas affect the facial structures, resulting in such conditions as

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medial canthal dystopia, elevated medial eyebrows and long nose deformities (Rojvachiranonda et al., 2006). An important pathology of the disease is that lesions may vary extensively from minor widening of the nasal root, to a very large protuberant mass eroding or displacing the medial orbital walls, or displacing the entire orbit laterally, when telecanthus or hypertelorism as defined by Tessier (Tessier, 1974) is present. Most previous studies have reported that FEEM was associated only with widening of the medial interorbital distance (MIOD) but the lateral interorbital distance (LIOD) was within normal limits (Jackson et al., 1983; David et al., 1984; Lello et al., 1989; Holmes et al., 2001). However, some studies stated that the LIOD might be widened (true hypertelorism) (Ortiz-Monasterio and Fuente-del-Campo, 1981; Fuente del Campo et al., 1989; Mahapatra 1997; Pinzer et al., 2008). In our institution, a widened LIOD in FEEM patients was observed. In addition, no report was identified in the literature regarding the incidence of hydrocephalus, microphthalmia or anophthalmia in FEEMs in northern Thailand. The aim of this study was to identify the prevalence of abnormal lateral interorbital distance (LIOD), microphthalmia or anophthalmia and hydrocephalus in frontoethmoidal encephalomeningocele (FEEM), and to identify the correlation between external bony defects and a widened lateral orbital wall.

2. Materials and methods

This retrospective cohort study was approved by the Ethics Committee of Faculty of Medicine, Chiang Mai University (CMU), ID 4829. The CMU Hospital database was assessed for FEEM between January 1, 2006, and December 31, 2016. Most of the patients were referred from Myanmar. The inclusion criteria included patients who were investigated using facial bone 3D CT imaging. We excluded any patients who had had prior facial surgery or maxillofacial bone trauma before they underwent a CT scan and also those with craniofacial disease such as facial clefts, frontonasal dysplasia, craniosynostosis, or interfrontal encephalocele. The patient characteristics included sex, age of the patient at the time of the CT scan, and types of FEEMs. Types of FEEMs were evaluated from CT imaging by a neuro-radiologist and a plastic surgeon. Facial bone CT scans were obtained using a Toshiba aquilion16, Siemens somatom definition and Siemens somation force CT scanner. All images were obtained using 0.625 to 1-mm slices, and soft tissue and bone windows were reviewed. Types of FEEMs were classified according to the criteria of Suwanwela and Suwanwela (Suwanwela and Suwanwela, 1972), Mahatumarat, and Taecholarn (Mahatumarat et al., 1991), and a new type, internasal type classification by Sirimaharaj (Sirimaharaj, 2018) (Table 1). The LIOD, MIOD and external bony defects were defined as described in Table 2 and Fig. 1. All of these diameters varied with age. Because our patients did not have a facial bone CT scan at the same age, we could not evaluate the true width of the external bony defect for prediction of a widened LIOD. Therefore, the proportion between the external bony defect and LIOD (EL ratio) was calculated instead of the true defect diameter. A cutoff value of the EL ratio was analyzed for prediction of a widened LIOD.

Table 1
Classification of frontoethmoidal encephalomeningoceles (FEEM).

Frontoethmoidal encephalomeningocele
Nasofrontal (NF)
Nasoethmoidal (NE)
Nasoorbital (NO)
Internasal (IN)
Combined
Abortive

Table 2
Computed tomography measurement of the craniofacial skeleton.

Measurement	Description
Lateral interorbital distance (LIOD)	The distance between the most anterior tip of each lateral orbital wall.
Medial interorbital distance (MIOD)	The distance between a point on each medial wall of the bony orbit.
External bone defect	Diameter of external bone defect was measured from imaging from axial, coronal or sagittal plane

Patients were divided into two groups: those with normal LIOD and those with wide LIOD. Wide LIOD was defined as a LIOD more than the mean LIOD +2 SD of the normal population in each age group, because, to date, there are no normal LIOD data in Thai children. The normal LIOD data were obtained from the study by Waitzman et al. (Waitzman et al., 1992).

The prevalences of hydrocephalus, microphthalmia, and anophthalmia were identified.

2.1. Measurements

1) We measured MIOD, LIOD from 0.625 to 1 mm-thick slice CT scans in the bone window. First, the orientation was in the Frankfurt horizontal plane as used in the study by Pool et al. (Pool et al., 2016). Following this, we advanced the transverse slices superiorly to the medial canthus and proceeded to use the workstation linear measurement tool to obtain the measurements. We chose an axial slice in the orbital region, transected the lens of the globe, the optic nerve, the ethmoid air cells, the nasal bones, and the superior aspect of the frontal process of the zygomatic bones (Waitzman et al., 1992). We proceeded to use the linear measurement tool to obtain the measurements of MIOD, LIOD and maximum external size of any bony defects in the axial plane.

2) Microphthalmia, anophthalmia, and presence of hydrocephalus were observed from the soft tissue window of the CT image. The International Clearinghouse for Birth Defects Monitoring Systems defines Anophthalmia as absent eyes and microphthalmia as small



Fig. 1. Measurements of MIOD, LIOD and external bony defect.

Table 3
Baseline characteristics of FEEMs (n = 94).

Characteristic	Wide LIOD (N = 13) n (%)	Normal LIOD (N = 81) n (%)	P-value
Sex			0.027
Male	12 (20.34)	47 (79.66)	
Female	1 (2.86)	34 (97.14)	
Age at CT scan* (months) median (iqr [#])	20 (11–76)	32 (8–115)	0.775
Type			0.543
Nasofrontal	1 (5)	20 (95)	
Nasoorbital	5 (20)	20 (80)	
Nasoethmoidal	0 (0)	9 (100)	
Internasal	1 (12.5)	7 (87.5)	
Combined	6 (19.35)	25 (80.65)	
MIOD (cm), (mean ± SD)	2.53 ± 0.53	2.77 ± 0.52	0.112
External bone defect (cm) (mean ± SD)	1.93 ± 0.81	1.54 ± 0.66	0.061
External bone defect: LIOD (%) (mean ± SD)	21.52 ± 9.20	18.99 ± 8.96	0.348
Microphthalmia/Anophthalmia	1 (11.11)	8 (88.89)	1.000
Hydrocephalus	7 (16.28)	36 (83.72)	0.562

eyes. Some normal adnexal elements may be present. Eyelids are usually present. Microphthalmia was diagnosed if the total axial length was at least twice the standard deviation below the mean for that age (Weiss et al., 1989).

Statistical analysis was carried out using a commercial statistical software package (STATA 15.1; StataCorp LP, College Station, TX, USA). Descriptive data were reported as a straight count and a percentage for categorical data. For continuous data, the mean and standard deviation or median and interquartile range were reported, depending on the data distribution. The univariable analysis was done using Fisher's exact test for categorical data and a Student's *t*-test or Mann–Whitney *U*-test for continuous data. Multivariable analysis was carried out to identify the prognostic factors for a wide LIOD by exponential risk regression and reported by adjusted risk ratio (RR) with 95% confidence interval clustering by type of FEEMs. The area under the receiver operating characteristic curve (AuROC) was plotted for assessing the performance of the multivariable model and a cutoff value of the EL ratio. The statistical significance level was set for a two-tailed approach with a *p*-value < 0.05.

3. Results

Data from 98 FEEM patients were included in the study. Excluded individual data were as follows: 1 patient with craniosynostosis, 2 with an interfrontal encephalocele and 1 where the operation for FEEM correction had taken place before the CT scan. Therefore 94 patients (59 male and 35 female) were included in the final analysis. The median patient age at the time of the CT scan was 2.65 years (range; 1 day to 45 years). There were 21 patients with the nasofrontal type FEEM, 25 with nasoorbital, 9 with nasoethmoidal, 8 with internasal, and 31 with combined type. Microphthalmia or anophthalmia in FEEMs was 9.57% and hydrocephalus was 45.74%. In all, 13 patients (13.83%) had a wide LIOD and 81 patients (86.17%) had a normal LIOD. The baseline characteristics between groups are shown in Table 3.

The univariable model showed that there were no statistically significant differences in terms of patient characteristics between the LIOD groups, apart from sex. Multivariable model showed that

male and EL ratio at 23% were significant (Table 4). The proportion of wide LIOD was higher in male patients as shown in Table 3. The optimal cutoff value of the EL ratio associated with wide LIOD was 23% as shown in Fig. 2. The sensitivity of this cutoff value was 46.2%, and the specificity was 74.1%. The positive predictive value (PPV) was 22.2% and negative predictive value (NPV) was 89.6%. The multivariable analysis indicated that factors associated with a wide LIOD were an EL ratio of 23% (adj RR = 1.98, 95% CI = 1.58–2.51) and male sex (adj RR = 6.85, 95% CI = 2.00–23.55) as shown in Fig. 2. Two examples of patients with wide LIOD are shown in Figs. 3 and 4.

4. Discussion

The results of this study demonstrated that the prevalence of a wide LIOD in FEEM patients in the north of Thailand accounted for 13.83% of cases, while previous studies showed rare true hypertelorism in FEEMs (Jackson et al., 1983; David et al., 1984; Lello et al., 1989; Holmes et al., 2001). Jackson et al. (Jackson et al., 1983) and David et al. (David et al., 1984) reported that most FEEMs exhibit telecanthus rather than teleorbitism and indicate that the lateral orbital walls are in a virtually normal position. A study by Fuente Del Campo et al. (Fuente del Campo et al., 1989) classified the facial deformity of FEEMs into three degrees. First-degree is associated with lateral displacement of the medial canthi and one or both medial wall of orbits. Second-degree is characterized by an upward displacement of the eyebrows or downward displacement of the tip of nose, giving the appearance of a long nose. Third-degree is the most severe form, involving the separation of one or both orbits from the midline, causing true orbital hypertelorism. Ortiz-Monasterio and Fuente-del-Campo (Ortiz-Monasterio and Fuente-del-Campo, 1981) reported a FEEM with a large encephalocele displacing the orbits, thereby resulting in true hypertelorism. They also mentioned that displacement of the entire orbit may occur when the volume of the intracranial content herniating through the bony gap is very large. Pinzer et al. (Pinzer et al., 2008) also found that 17% (10 in 58 patients) with FEEMs showed true hypertelorism. Hemmy et al. (Hemmy and David, 1985) reported that the defects associated with FEEM are like blowout defects, which displace

Table 4
Multivariable analysis of factors associated with abnormal LIOD clustered by type of FEEMs.

Characteristics	Crude risk ratio (95% confidence interval)	P-value	Adjusted risk ratio (95% confidence interval)	P-value
EL ratio at 23%	2.12 (1.50–3.00)	<0.001	1.98 (1.57–2.50)	<0.001
Sex (Male over female)	7.11 (2.13–23.69)	0.001	6.85 (1.99–23.54)	0.002

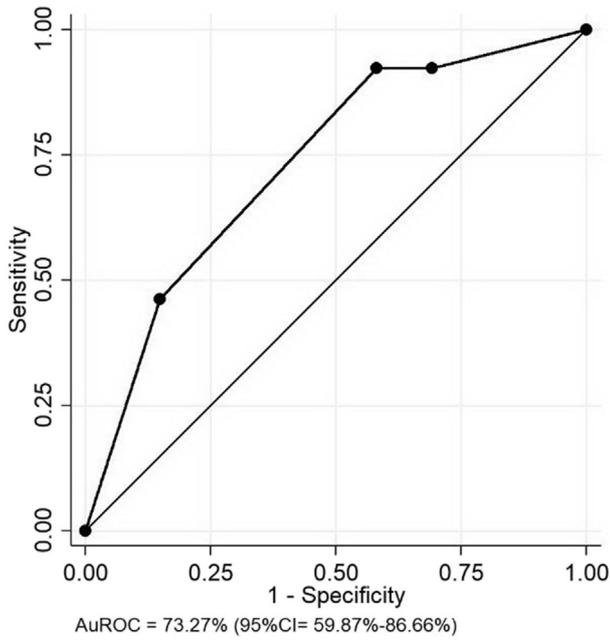


Fig. 2. ROC curve of the model of prognostic indicators for wide LIOD in FEEMs predicted by EL ratio of 23% (curved line) and a 50% chance prediction (diagonal line).

otherwise normal orbits and nasal capsules, widening the orbits (however that study did not specify clearly which orbital walls were widened). This information supported our results.

In this study, sex was one of the significant factors for the prediction of a wide LIOD. A study has been carried out in a normal population (one with no FEEM history) using CT scanning regarding normal values of craniofacial parameters. Unfortunately this was not stratified by sex (Waitzman et al., 1992). Further studies into the different values of craniofacial parameters between the sexes are warranted.

Most patients in the wide LIOD group in our study showed the combined type, which was the same clinical finding of FEEMs reported in Pinzer et al.'s study (Pinzer et al., 2008). Pinzer reported hypertelorism as a generalization of the bony and soft tissues of the orbits (excessive inner canthal, outer canthal and interpapillary distance) in the nasoethmoidal-nasoorbital type.

The diameter of external bony defects in the wide LIOD group is greater than that found in the normal group. Although we could not demonstrate statistically significant differences in this study, with a larger sample size the wider defect may well be associated with a wide LIOD. The larger defects were associated with more severe facial deformities (Rojvachiranonda et al., 2003). As the population in our study was not within a distinct age group, measurements would vary a great deal with age, and the exact value of the true bony defect could not be used to give a generalized direct estimate for a wide LIOD. We evaluated the EL ratio (the proportion between

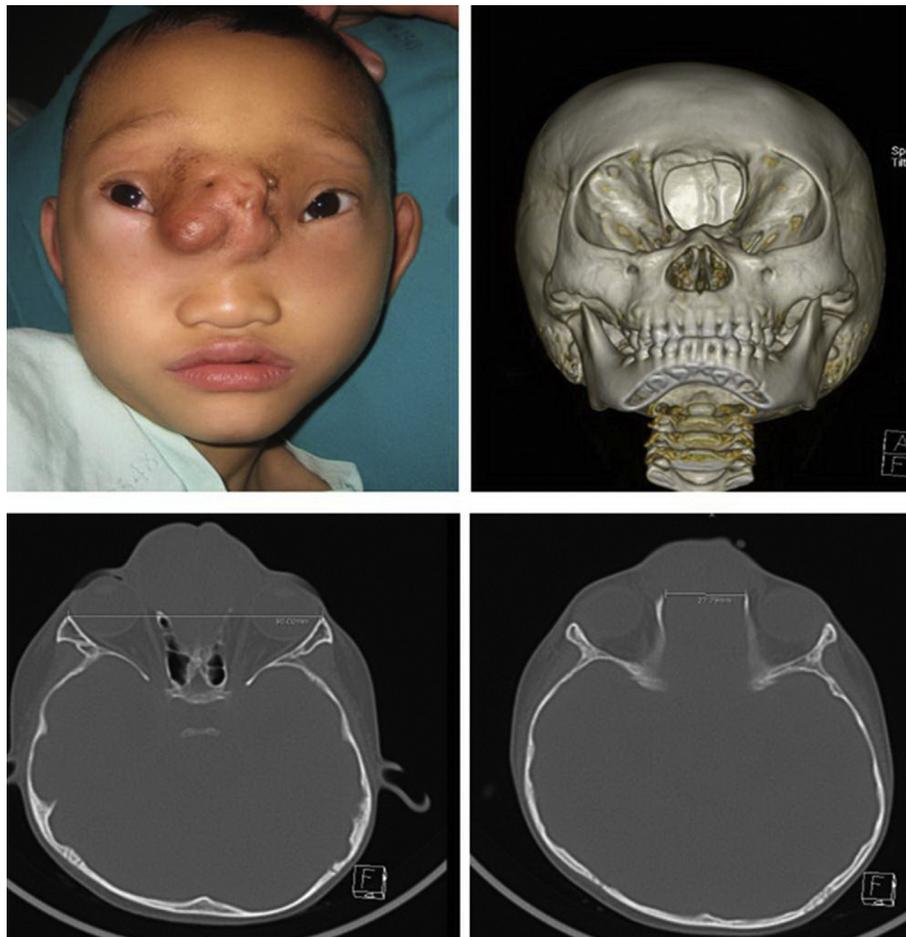


Fig. 3. A 4 year old girl with Internasal and bilateral Nasoorbital type FEEM with wide LIOD, EL ratio = 27.79/90.02 = 30.87.



Fig. 4. A 4 month old boy with Internasal type FEEM with wide LIOD, EL ratio = $23.68/85.33 = 27.75$.

the external bony defect and LIOD) instead. In this study, a cutoff value of 23% was used for predicting a wide LIOD.

In this study, the majority of incidences of microphthalmia and anophthalmia were detected in the naso-orbital and combined (naso-orbital and nasoethmoidal) types. These signify that a mass that herniates through the orbit causes abnormalities. The prevalence of microphthalmia and anophthalmia in our study (northern Thailand) was higher than that reported in Nond's study (Rojvachiranonda et al., 2003) in Southeast Asia (9.57% versus 4.4%).

One study indicated that hydrocephalus without clinical signs of increased intracranial pressure can be found in FEEMs (Hoving and Vermeij-Keers, 1997). In our study, hydrocephalus was found in almost half of FEEMs (45.74%, 43 of 94), and 34.88% of them were symptomatic and required drainage by a ventriculo perineal shunt.

Currently the most frequently used surgical correction of the FEEMs is the Chula technique in which repairs and reconstruction for FEEMs are performed in one stage (Mahatumarat et al., 1991). This technique reduces the interorbital distance by shifting the superomedial orbital walls medially and securing them by interosseous wiring. Some previous studies reported that in most FEEMs only the distance between medial orbital walls was increased to within a normal lateral orbital wall distance, so medial translocation of the medial orbital wall with medial canthopexy is preferred (David et al., 1984; Lello et al., 1989; Pinzer et al., 2008). Nevertheless, we observed a wide LIOD in FEEM patients, which was related to the diameter of the external bony defect. More than 23% of the EL ratios helped to moderately predict a wide LIOD. This leads to an increasing awareness of craniofacial skeletal abnormalities, and guides physical examinations and treatment plans. Even though Pizer et al. stated that half of hypertelorism patients (5 of 10) had an improvement in the LIOD after surgery without correction of the lateral orbit, there were still some patients who showed no improvement. One possible reason may be due to attainment of maximum facial size in adult patients. In the future, however, panorbital translocation may be carried out to improve facial balance and to reduce psychological morbidity of an appearance difference.

Limitations of this study were that it was of a retrospective nature, and also no normal values were referenced in Asian anthropomorphic measurements. Future studies with a larger number of patients should be carried out. Also a separate study to create a database of normal values of Asian anthropomorphic measurements should be completed.

5. Conclusion

Although frontoethmoidal encephalomeningoceles are predominantly associated with the telecanthus, a wide LIOD could be found in some FEEMs. This indicated true orbital hypertelorism. A

relationship between the external bony defect and the widening of the lateral orbital wall was observed. More than 23% of the EL ratios could be used to predict an abnormal LIOD with moderate confidence. A more complex panorbital translocation in FEEMs with hypertelorism may attain normalization of facial appearance. Thus, the preoperative work-up should include precise differentiation between the two phenomena of telecanthus and hypertelorism. Results from the evaluation of orbital measurement values may be used for preoperative planning. The results provide essential information for successful surgical correction in FEEMs in efforts to obtain the best facial appearance.

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Conflicts of interest

The author declared that there is no conflict of interests.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.jcms.2019.07.013>.

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