Ultrasound Obstet Gynecol 2015; **46**: 665–669
Published online 8 November 2015 in Wiley Online Library (wileyonlinelibrary.com). **DOI:** 10.1002/uog.15675

Maxillary gap at 11–13 weeks' gestation: marker of cleft lip and palate

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KEYWORDS: cleft lip; cleft palate; maxillary gap

ABSTRACT

Objective *To describe a new sign of cleft lip and palate (CLP), the maxillary gap, which is visible in the mid-sagittal plane of the fetal face used routinely for measurement of nuchal translucency thickness.*

Methods *This was a retrospective study of stored images of the mid-sagittal view of the fetal face at 11–13 weeks' gestation in 86 cases of CLP and 86 normal controls. The images were examined to determine if a maxillary gap was present, in which case its size was measured.*

Results *In 37 (43.0%) cases of CLP the defect was isolated and in 49 (57.0%) there were additional fetal defects. In the isolated CLP group, the diagnosis of facial cleft was made in the first trimester in nine (24.3%) cases and in the second trimester in 28 (75.7%). In the group with additional defects, the diagnosis of facial cleft was made in the first trimester in 46 (93.9%) cases and in the second trimester in three (6.1%). A maxillary gap was observed in 96% of cases of CLP with additional defects, in 65% of those with isolated CLP and in 7% of normal fetuses. There was a large gap (>1.5 mm) or complete absence of signals from the maxilla in the midline in 69% of cases of CLP with additional defects, in 35% of those with isolated CLP and in none of the normal controls.*

Conclusions *The maxillary gap is a new simple marker of possible CLP, which could increase the detection rate of CLP, especially in isolated cases.* *Copyright © 2015 ISUOG. Published by John Wiley & Sons Ltd.*

INTRODUCTION

Cleft lip and palate (CLP) is a common congenital defect that can be either isolated or associated with a wide range of chromosomal abnormalities and genetic syndromes. Isolated cleft lip or cleft palate may escape prenatal detection, but combined CLP is diagnosed easily during the routine second-trimester scan[1,2].

In the last decade, widespread use of the 11–13-week scan in screening for aneuploidies with measurement of fetal nuchal translucency (NT) thickness has resulted in many major fetal defects being diagnosed in the first trimester of pregnancy[3]. This can be achieved by direct visualization of the fetal anatomy, for example in cases of anencephaly, exomphalos and megacystis[3], or by focused assessment of specific fetal structures triggered by the finding of indirect signs, for example increased NT in association with major cardiac defects[4,5] and abnormal intracranial translucency (IT) in association with open spina bifida[6–9].

Most cases of CLP are not detected during the first-trimester scan[3]. Improved detection may be achieved by targeted examination of the face in a coronal view and assessment of the retronasal triangle[10]. However, the uptake of such assessment may be limited by the necessity to include examination of a plane additional to the standard mid-sagittal view that is necessary for measurement of fetal crown–rump length, NT, nasal bone (NB) and IT.

The objectives of this study were first, to describe a new sign of CLP, the maxillary gap, visible in the mid-sagittal plane of the fetal face, which is used routinely for measurement of NT, NB and IT (Figures 1 and 2) and, second, to provide preliminary data on the potential value of the maxillary gap in the early diagnosis of CLP.

SUBJECTS AND METHODS

In three cases of CLP we made an incidental observation that, in the mid-sagittal view of the fetal face at 11–13 weeks' gestation, there was a gap in the echogenic line representing the palate; no such gap was observed in 10 consecutive cases of normal fetuses. We therefore subsequently conducted a search of the databases of

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Accepted: 11 August 2015

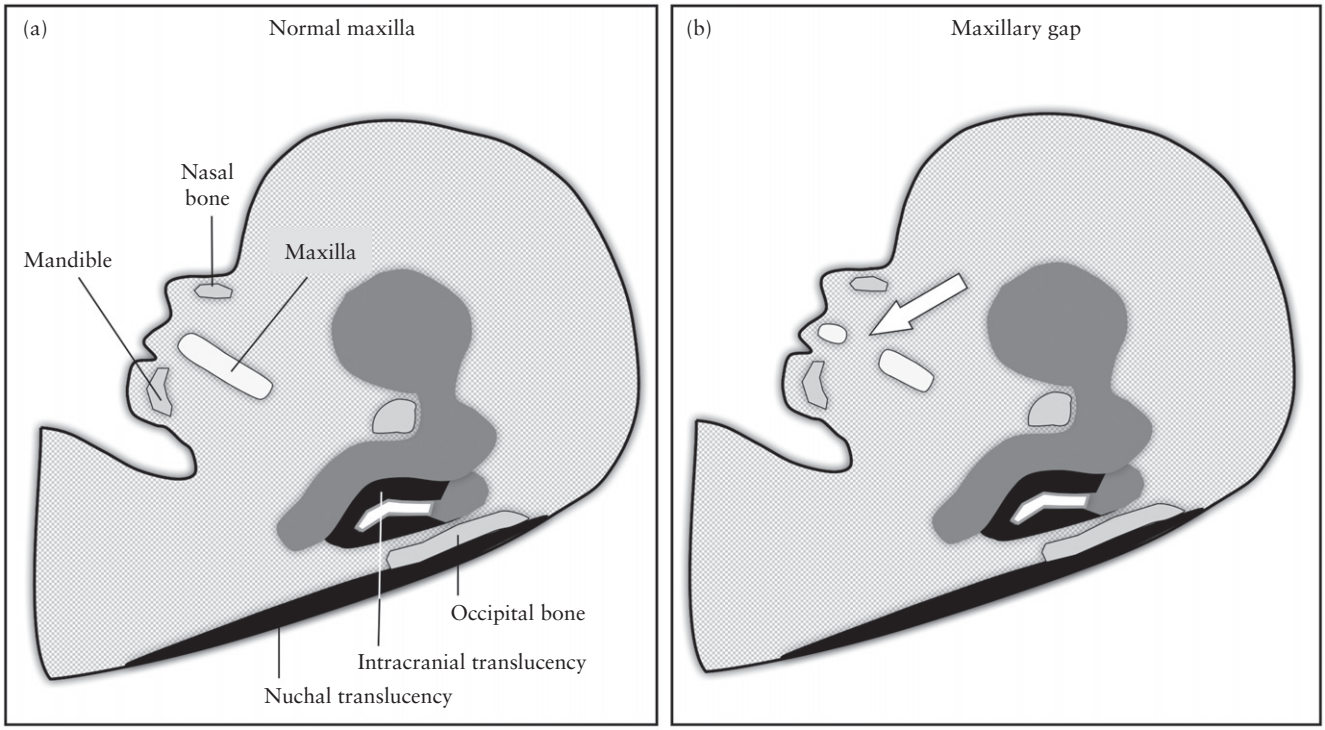

Figure 1 Standard mid-sagittal view of the fetal face used routinely at 11–13 weeks, illustrating the maxilla in a normal fetus (a) and the maxillary gap (open arrow) in a fetus with cleft lip and palate (b).

two major centers of prenatal diagnosis, to identify fetuses with CLP which underwent routine first-trimester screening for aneuploidies. The stored images of the mid-sagittal view of the face in these cases were retrieved and for each case a control was selected: a fetus examined on the same day that was subsequently liveborn without any abnormality.

The diagnosis of CLP was made in a coronal view of the face. In most cases which underwent termination of pregnancy, diagnosis was confirmed clinically or at autopsy. Cases with isolated cleft lip or cleft of the posterior palate were not included in the study. Transabdominal ultrasound examinations were performed initially as part of routine NT screening and, in the presence of fetal malformations, an additional transvaginal examination was performed selectively.

All retrieved images of cases and controls were assessed offline by two independent examiners (R.C., G.O.) who were unaware of the final diagnosis. The images were examined to determine if a maxillary gap was present; if this was the case we determined whether it was partial or complete (Figure 2) and measured the size of the gap. Ultrasound findings and pregnancy outcome data were obtained from the databases and their relation to the maxillary gap was examined.

RESULTS

The study population comprised 86 cases of CLP with satisfactory images of the mid-sagittal view of the fetal face at 11–13 weeks, identified from the combined databases of the two centers. The characteristics of the study population and controls are summarized in Table 1. In the controls no defect was detected in either the first- or the second-trimester scan and all pregnancies resulted in healthy live births with no defects.

The diagnosis of facial cleft was made in the first trimester in 55 (64.0%) and in the second trimester in 31 (36.0%) of the CLP cases (Table 1). The diagnosis was suspected in the first trimester in some cases due to maxillary protrusion or to the presence of associated anomalies and was confirmed by examining a coronal view of the face and the oblique view of the retronasal triangle.

In 37 (43.0%) cases the facial cleft was an isolated finding; in three (8.1%) of these the pregnancy was terminated at the request of the parents, one (2.7%) underwent neonatal death due to birth asphyxia and in 33 (89.2%) the pregnancy resulted in live birth and the infant underwent surgery for correction of the defect. In this group with isolated CLP the diagnosis of facial cleft was made in the first trimester in nine (24.3%) cases and in the second trimester in 28 (75.7%).

In 49 cases of CLP there were additional fetal defects. In 47 cases fetal karyotyping following chorionic villus sampling or amniocentesis was carried out; the karyotype was normal in 12 (25.5%) and abnormal in 35 (74.5%), including 23 cases of trisomy 13, nine of trisomy 18 and three other chromosomal abnormalities. In 45 cases the pregnancy was terminated at the request of the parents, two fetuses died *in utero* and in two the pregnancy resulted in live birth and the infant underwent surgery for correction of the defect. In this group with additional

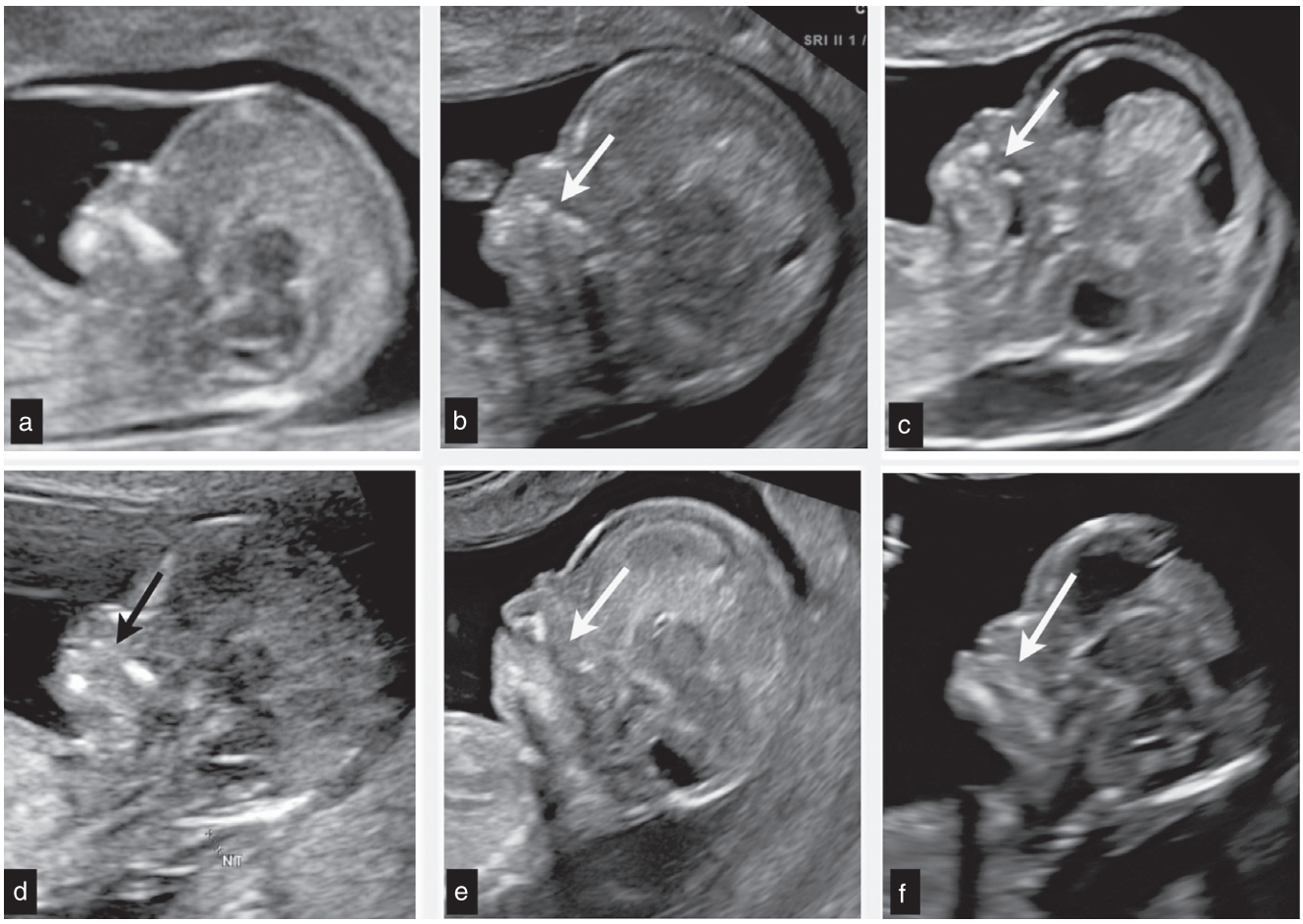

Figure 2 Ultrasound images in the mid-sagittal plane of the face in a normal fetus with no maxillary gap (a), a normal fetus with small maxillary gap (arrow) (b) and four fetuses with cleft lip and palate, showing partial (c,d,e) or complete (f) maxillary gap (arrows).

defects the diagnosis of facial cleft was made in the first trimester in 46 (93.9%) cases and in the second trimester in three (6.1%).

A maxillary gap was observed in six (7.0%) of the controls, in 24 (64.9%) cases with isolated CLP and in 47 (95.9%) cases of CLP with additional abnormalities (Table 2). Figure 2 illustrates partial and complete maxillary gaps. The size of the gap in all six controls was < 1.5 mm. Of the 24 cases of isolated CLP with a maxillary gap, its size was < 1.5 mm in 11 (45.8%) and 1.5–5.0 mm in 13 (54.2%). Of the 47 cases with CLP, additional defects and a maxillary gap, the gap size was < 1.5 mm in 13 (27.7%), 1.5–5.0 mm in 21 (44.7%) and complete in 13 (27.7%); in eight of the latter fetuses there was holoprosencephaly and a median facial cleft.

Protrusion of the maxilla in the profile view was observed in 20 (40.8%) of the 49 fetuses with CLP and additional abnormalities and in seven (18.9%) of the 37 cases with isolated CLP (Table 1).

DISCUSSION

This study demonstrates that CLP can be suspected at 11–13 weeks' gestation in the presence of a maxillary gap in the standard mid-sagittal view of the fetal face that is used routinely in screening for chromosomal abnormalities. A maxillary gap was observed in 96% of cases of CLP with additional abnormalities, in 65% of those with isolated CLP and in 7% of normal fetuses. There was a large gap or complete absence of signals from the maxilla in the midline in 69% of cases of CLP with additional abnormalities, in 35% of those with isolated CLP and in none of the normal controls.

At the end of complex embryological development of the midline of the face between 6 and 12 weeks' gestation, the nose and lip are formed and the palate closes. Anatomically, the palate is then composed of three parts: the anterior or primary palate, including the alveolar ridge, the posterior or secondary palate and the soft palate[11]. At the time of the 11–13-week scan, some parts of the maxilla may still show lack of ossification. This may explain the finding of a gap in some of the normal controls: in all of these, the size of the suspected gap was very small (< 1.5 mm). Therefore, suspicion of a small maxillary gap in the mid-sagittal view in the presence of an intact maxilla in the coronal view can be considered as a normal finding.

The diagnosis of CLP was made at the 11–13-week scan in 94% of the cases with other abnormalities, but in only 24% of those with isolated CLP. This is not surprising

Table 1 Characteristics of study group of 86 fetuses with facial cleft and 86 normal controls

Characteristic	*Normal controls (n = 86)*	*Facial cleft*	
		Isolated (n = 37)	*Other defects (n = 49)*
Maternal age (years)	32 (30–36)	32 (26–35)	34 (28–39)
Gestational age (weeks)	12.6 (12.3–12.7)	13.0 (12.7–13.3)	12.7 (12.1–13.3)
Crown–rump length (mm)	61.0 (57.3–64.0)	68.3 (63.5–72.9)	60.2 (54.6–68.3)
Nuchal translucency thickness (mm)	1.6 (1.4–1.9)	1.9 (1.7–2.1)	2.8 (1.9–4.9)
Fetal karyotype			
Normal or normal live birth	86 (100)	37 (100)	12 (24.5)
Trisomy 13	—	—	23 (46.9)
Trisomy 18	—	—	9 (18.4)
Other	—	—	3 (6.1)
Unknown	—	—	2 (4.1)
Cleft location			
Median	—	—	12 (24.5)
Bilateral	—	7 (18.9)	26 (53.1)
Unilateral	—	30 (81.1)	11 (22.4)
Maxillary protrusion	—	7 (18.9)	20 (40.8)
Time of diagnosis			
First trimester	—	9 (24.3)	46 (93.9)
Second trimester	—	28 (75.7)	3 (6.1)
Outcome			
Live birth	86 (100)	33 (89.2)	2 (4.1)
Neonatal death	—	1 (2.7)	—
Termination of pregnancy	—	3 (8.1)	45 (91.8)
Fetal death	—	—	2 (4.1)

Data are given as median (interquartile range) or *n* (%).

Table 2 Type and size of maxillary gap in 86 fetuses with facial cleft and 86 normal controls

Maxillary gap characteristic	*Normal controls (n = 86)*	*Facial cleft*	
		Isolated (n = 37)	*Other defects (n = 49)*
Type			
No gap	80 (93.0)	13 (35.1)	2 (4.1)
Partial gap	6 (7.0)	24 (64.9)	34 (69.4)
Complete gap	—	—	13 (26.5)
Size			
< 1.5 mm	6 (100)	11/24 (45.8)	13/47 (27.7)
1.5–5 mm	—	13/24 (54.2)	21/47 (44.7)
Complete	—	—	13/47 (27.7)

Data are given as *n* (%).

because, in the presence of often multiple sonographic defects, a systematic search is undertaken for additional defects, including CLP, especially in cases with suspected trisomy 18 or 13.

Examination of the maxilla in the mid-sagittal view of the fetal face at 11–13 weeks has been reported previously, in studies which focused mainly on its length in normal fetuses and in fetuses with trisomy 21 or on its use as a landmark for calculation of the frontomaxillary facial angle[12–15]. Our present study emphasizes a new aspect of early assessment of the maxilla: looking for a maxillary gap as a potential marker of CLP.

In the prenatal diagnosis of facial cleft the typical recommended views during the second-trimester scan are the axial view of the maxilla and the coronal view of the nose and lip[11,16,17]. The importance of the mid-sagittal view of the palate was reported recently for demonstration of the so-called 'equals sign' corresponding to the anatomical appearance of the soft palate and uvula[18]. It was suggested that, in the first trimester, identification of cleft palate necessitates a coronal view of the anterior bony face and demonstration of the retronasal triangle[10]. Some studies have reported on the use of the retronasal triangle view with three-dimensional (3D) ultrasound to demonstrate CLP and retrognathia[19–22]. However, the retronasal triangle plane on two-dimensional (2D) or on 2D in combination with 3D ultrasound has not been accepted widely as a standard view in routine screening. In contrast, we have highlighted the importance of the maxillary gap as a marker of possible CLP because the marker is visible in the standard plane that is obtained routinely in screening for aneuploidies.

The main strength of the study is the large number of affected cases with stored images of quality acceptable for assessment. The main limitation relates to its retrospective nature and reliance on stored images. Although for the cases of CLP detected in the first trimester there were numerous images and video recordings, for those in which the diagnosis was missed there were only a few stored images for assessment.

In conclusion, examination of the mid-sagittal view of the fetal face, which is performed routinely for assessment of fetal NT, NB and the posterior brain region, can identify a maxillary gap and lead to first-trimester diagnosis of CLP. In cases of maxillary gap, the sonographer should undertake detailed examination of the face and palate regions. Prospective large studies are necessary to determine the performance of the maxillary gap in screening for facial clefts.

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