Prenatal diagnosis of congenital head, face, and neck malformations—Is complementary fetal MRI of value?

Roni Zemet1,2 | Inna Amdur-Zilberfarb2 | Moran Shapira1,2 | Tomer Ziv-Baran3 | Chen Hoffmann2,4 | Eran Kassif1,2 | Eldad Katorza1,2

1 Department of Obstetrics and Gynecology, Sheba Medical Center, Ramat Gan, Israel
2 Sackler School of Medicine, Tel Aviv University, Tel Aviv, Israel
3 School of Public Health, Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel
4 Department of Diagnostic Radiology, Sheba Medical Center, Ramat Gan, Israel

Correspondence
Roni Zemet, MD, Department of Obstetrics and Gynecology, Sheba Medical Center, Tel-Hashomer, Ramat Gan, Israel.
Email: ronizemet@gmail.com

Abstract

Objectives: The aim of this study was to evaluate the role of fetal magnetic resonance imaging (MRI) as a complement to ultrasound (US) in the prenatal diagnosis of craniofacial anomalies.

Methods: A historical cohort study including all pregnant women who were referred for fetal MRI because of antenatal diagnosis of craniofacial anomalies on screening US. Prenatal diagnostic US, MRI, and postnatal diagnosis were compared for consistencies and discrepancies.

Results: Forty-five pregnant women with 73 suspected fetal craniofacial anomalies diagnosed by US underwent MRI. In 40 out of 73 anomalies (54.8%), US and MRI findings were in complete agreement with postnatal diagnoses. MRI correctly ruled out the diagnosis of 24 anomalies suspected on US and diagnosed four additional pathologies that were not demonstrated by US. Out of the 85 anomalies (suspected by imaging or confirmed postnatally), confident diagnosis could be made by MRI in 68 anomalies (80%), not diagnosed in 10 (11.8%), and over-diagnosed in seven (8.2%). By US, confident diagnosis could be made in 44 anomalies (51.8%), not diagnosed in 11 (12.9%), and over-diagnosed in 30 (35.3%).

Conclusion: MRI is valuable in the antenatal evaluation of fetal craniofacial anomalies and may be useful as an adjunct to US in the prenatal work-up of craniofacial anomalies.

1 | INTRODUCTION

Fetal craniofacial anomalies produce various degrees of disfigurement and can result in severe functional impairment postnatally. Craniofacial anomalies represent one of the most challenging prenatal diagnoses, mainly because of the wide range of morphological features involved. However, owing to improvement in prenatal diagnosis through ultrasonography (US) and magnetic resonance imaging (MRI), the approach to fetuses with craniofacial anomalies has shifted from diagnosis at birth with emergency measures taken as needed, to prenatal diagnosis that facilitates parents’ counselling, evaluation of genetic etiologies, and careful planning of delivery and postnatal treatment.

US is the primary imaging modality for fetal assessment. It is safe, allows multiplanar and real-time imaging, is relatively inexpensive, and readily available. US can detect orofacial clefts, cervicofacial masses, the vascularity of such masses, and to a certain extent upper airway obstruction as measured by polyhydramnios. Nonetheless, US accuracy may be limited by factors such as oligohydramnios, maternal body
habitus, complex fetal anomalies, fetal position and overlying limbs, advanced gestational age, or the skills of the performing operator.\(^3\)

The evaluation of the head, face, and neck can be limited by superimposition of the tongue and the acoustic shadowing caused by ossification of facial structures.\(^5\) In these cases, alternative imaging modalities may provide additional information that can improve diagnostic accuracy and facilitate treatment decisions.

MRI has progressively emerged as a valuable adjunct to US in the work-up of fetal craniofacial pathology because of the development of ultrafast sequences that have few motion artefacts and offer excellent spatial resolution.\(^5-7\) Fetal craniofacial anomalies described on MRI include clefts, retrognathia, micrognathia, craniosynostosis, cephaloceles, vascular anomalies, tumors, dacryocystoceles, ocular, and orbital abnormalities.\(^5,8\) Although the role of MRI as a complement to US in the diagnosis of cleft lip and palate has been established,\(^4,7,9\) the data regarding its efficacy in evaluation of other craniofacial anomalies is limited.

The aim of the present study was to evaluate the role of fetal MRI as a complement to US in prenatal diagnosis of head, face, and neck anomalies, through comparing antenatal sonography and MRI findings with physical examination and postnatal imaging.

## METHODS

### 2.1 Study population

This historical cohort included all pregnant women who were referred for fetal MRI because of suspected head, face, or neck anomalies diagnosed by US between January 2011 and July 2016 in a single university-affiliated tertiary referral hospital. Demographic and clinical data were collected from the electronic records of the mother and neonate. Any missing data were gathered through direct phone interviews with the women.

In order to explore the validity of MRI in the diagnosis of craniofacial anomalies through calculation of sensitivity, specificity, and diagnostic accuracy, an additional cohort of women who were referred for fetal MRI for indications other than suspected head, face, or neck malformations was established. The MR studies of this cohort were used as a data source, and the images were not reevaluated for the current study. The study was approved by the Institutional Review Board of our institution (no. 1725-14-SMC).

### 2.2 Imaging technique and interpretation

All patients underwent expert diagnostic antenatal ultrasound, fetal MRI, and were advised to have an amniocentesis for karyotype analysis.

#### 2.2.1 Ultrasound

All women underwent anatomical US screening tests performed by an obstetrical sonography specialist according to the International Society of Ultrasound in Obstetrics and Gynecology (ISUOG) guidelines. Most fetuses with a craniofacial anomaly were diagnosed by an earlier anatomical US screening test performed by an obstetrics sonography specialist at 14 to 17 or 20 to 24 weeks of gestation for early or late assessment, respectively. Some fetuses were diagnosed during the third trimester because of lack of adequate maternal compliance during earlier pregnancy stages or inadequate diagnosis of a craniofacial anomaly during earlier screening examinations. Following the US screening test, complete fetal surveys (targeted US) were performed by very experienced sonographers at our referral center with additional dedicated views of the profile, lips, face, and neck. All fetuses underwent brain US evaluation, including of the head shape, lateral ventricles and choroid plexus, cerebellum, cisterna magna, thalami, and cavum septi pellucidi as visualized in the trans-ventricular plane, trans-cerebellar plane, and trans-thalamic plane, again according to the ISUOG-guidelines.\(^10\)

#### 2.2.2 Magnetic resonance imaging

MRI is routinely performed in our institution once a congenital craniofacial anomaly is suspected on US. All patients underwent hence an MRI study of the fetal face and central nervous system. Although fetal MRI of the head, face, and neck can be performed during the second or third trimester, the preferred timing for fetal MRI in our institute is the 32nd week of gestation because at that time one can also assess brain maturation, parenchyma, and make a comprehensive brain structural assessment.\(^11\) In cases of later craniofacial anomalies diagnosis, MRI was conducted within a few days of diagnosis. All patients routinely signed an informed consent form prior to MRI performance.

Fetal MRI was performed using a 1.5-Tesla system (Optima scanner, GE Healthcare Technologies, Milwaukee, Wisconsin) as previously described.\(^12,13\) The anatomic area was mapped, and sequence selection and planes of acquisition were chosen according to sonographic findings and clinical context, as defined by a neuro-radiologist MRI expert (C.H.). Images were acquired in three orthogonal planes with respect to the fetal face. The sagittal view provides a good evaluation of the fetal profile, including the frontal and nasal bones, hard palate, tongue, and mandible. A coronal view is useful in assessing the integrity of the fetal lips and palate, as well as providing delineation of the
eyes, nose, and ears. Axial view helps assess the different compartments of the neck and is also valuable in evaluating the fetal facial structures and variations in cranial morphology. In addition to morphological analysis, detailed brain biometry was performed using standard reference data. All MRI scans were assessed by a joint MRI and US team, which included a specialist in fetal US (E.K.) and a neuroradiologist MRI expert (C.H.).

2.3 Outcome measurements

US and MR images interpretations were compared for consistencies and discrepancies. US and MR imaging were categorized as correct or incorrect with respect to the final postnatal diagnosis, which was considered the reference standard. Postnatal diagnosis was obtained through physical examination, plain radiograph, US, computed tomography, MRI, surgery, or fetal autopsy in cases of termination of pregnancy. In addition, we noted cases in which MRI or US provided more information.

2.4 Statistical analysis

The normality of distribution of continuous variables was tested by histogram and Q-Q plots. Continuous variables with normal distribution are presented as mean and standard deviation (SD); non-normal distributed continuous variables are presented as median and interquartile range (IQR). Categorical variables are reported as number and percentage. Continuous variables normally distributed were compared using Student t test, and Mann-Whitney test was used to compare continuous variables not normally distributed. Categorical variables were compared using Chi-square test or Fisher exact test, as appropriate. Agreement between US and MRI findings was measured using kappa-statistics (k). According to Landis and Koch, the kappa values were interpreted as follows: 0.81 to 1.00 = almost perfect agreement, 0.61 to 0.80 = substantial agreement, 0.41 to 0.60 = moderate agreement, 0.21 to 0.40 = fair agreement, 0 to 0.20 = poor agreement, and 0 = no agreement. The sensitivity, specificity, and diagnostic accuracy of MRI and US were evaluated with postnatal diagnosis as a standard of reference. A two-tailed P < .05 was considered statistically significant. Analyses were performed with SPSS version 24.0 for windows (SPSS Inc., IBM Corp., Armonk, New York).

3 RESULTS

3.1 Demographic and clinical characteristics of the study populations

Sixty-four pregnant women with fetuses suspected to have craniofacial anomalies based on screening US were referred for fetal MRI in our institution over a 6-year period (2011-2016). Following preliminary record review and complementary phone interviews, 19 women were excluded: five women declined to participate in the study, three women performed termination of pregnancy without autopsy, and 11 patients were found to have incomplete records. Thus, the study group comprised a total of 45 pregnant women who underwent fetal MRI scans: 44 singleton pregnant women and one dichorionic diamniotic twin pregnancy with a single affected fetus. The control cohort comprised 61 pregnant women who were referred for fetal MRI for other indications. Final diagnosis was obtained from all fetuses at postnatal physical examination (n = 99) or at autopsy (n = 7).

The average gestational age of the study group at the time of prenatal MRI was 31.6 (SD 4.8; range 22-41). Twenty-nine (64.4%) fetuses were male and 16 were female. The median gestational age at diagnosis of face or neck anomalies on US was 22.57 (IQR 16-29). Targeted US and MRI were performed at average gestational age of 29 (range 18-37) and 31.71 (range 24-37), respectively. Twenty-six (57.8%) women had undergone amniocentesis, and six fetuses had abnormal array comparative genomic hybridization. In controls, all fetuses were evaluated by both early and late US screening survey performed at 14 to 17 and 20 to 24 weeks of gestation, respectively. Mean gestational age at time of fetal MRI was 32.86 (range 31.43-35), which was significantly higher than that of the study group (P = .03).

Table 1 displays the demographic and clinical characteristics of the study and comparison cohort. In controls, all mothers and partners had no family history of genetic disorders or syndromes compared with four (8.9%) patients in the study group (P = .03). Other demographic and clinical characteristics, including median maternal age, obstetric history, current fetal gender, maternal history of chronic medical conditions or surgical history, exposure to medication, smoking, alcohol or recreational drugs, and family history of congenital anomalies, did not differ statistically between the groups.

In the study group, 45 women with fetuses with 73 suspected craniofacial anomalies were referred for fetal MRI. The indications for fetal MRI included: cleft lip (n = 15) and palate (n = 14), cysts/masses/tumors of the face or neck (n = 6), hypotelorism/hypertelorism (n = 5), micrognathia/retrognathia (n = 5), prenasal and frontal edema (n = 5), forehead structure anomalies (n = 3), ear structure anomalies (n = 3), nuchal edema (n = 3), skull cysts (n = 3), tracheoesophageal malformations (n = 2), craniosynostosis (n = 2), and meningoencephalocele (n = 1).

3.2 Comparison of US versus MRI, stratified by malformations

3.2.1 Cleft lip

In 14 (93.3%) of 15 cases with cleft lip suspected initially on US, the diagnoses established by both US and MRI were correct when compared with postnatal diagnosis. In one case, MRI refuted the diagnosis of cleft lip, and this was confirmed by pediatric examination.

3.2.2 Cleft palate

Fourteen cases with cleft palate suspected on US were referred to fetal MRI. MRI confirmed the diagnoses in eight cases, and the diagnoses established by both imaging techniques were correct postnatally. Discrepancies occurred in 10 cases; in these cases, the diagnosis on
US was rejected by MRI, and the MRI interpretation was correct. MRI raised suspicion for cleft palate in four additional cases, and diagnosis was confirmed by pediatric examination in only three cases (Figure 1).

### 3.2.3 Cysts/masses/tumors of the face or neck

There were six cases with cervicofacial cysts or tumors. MRI confirmed the diagnosis in four, and these diagnoses were correct when compared with postnatal diagnosis: pharyngeal teratoma, namely, epignathus (Figure 2); lymphatic malformation in a cheek; macrocystic lymphatic malformation in the posterior triangle of the neck; and an astrocytoma behind one eye. In two cases, diagnosis at US was rejected by MRI, the latter interpretation being correct after birth.

### 3.2.4 Eye structure anomalies

Six cases with structural eye anomalies on US were referred for MRI: microphthalmia, anophthalmia, irregular structure of the eyeball, retinal detachment, and opaque lenses. MRI confirmed the diagnosis in

---

**TABLE 1** Demographic and clinical characteristics of study and comparison groups

| Characteristic                                      | Study Group—Cervicofacial Anomalies Anomaly (n = 45) | Comparison Group (n = 61) | P value |
|-----------------------------------------------------|------------------------------------------------------|---------------------------|---------|
| Maternal age, y                                      | 31.6 (28-35.5)                                       | 31.5 (29-35)              | .92     |
| Gravidity                                           | 2.7 (1-4)                                           | 2.6 (2-3)                 | .65     |
| Parity                                              | 1.2 (0-2)                                           | 1.1 (0-2)                 | .97     |
| Background of genetic disorder or syndromes, n (%)  | 4 (8.9%)                                             | 0                         | .03     |
| Mode of conception                                   |                                                      |                           |         |
| Spontaneous                                         | 37 (82.2%)                                          | 52 (85.2%)                | .74     |
| COH                                                 | 3 (6.7%)                                            | 2 (3.3%)                  |         |
| IVF                                                  | 5 (11.1%)                                           | 7 (11.5%)                 |         |
| Fetal gender (male)                                  | 29 (64.4%)                                          | 31 (51%)                  | .17     |
| Normal nuchal translucency scan                      | 2 (4.8%)                                            | 1 (1.6%)                  | .16     |
| Gestational age at diagnosis by US (weeks)          | 22.57 (16-29)                                       |                           | -       |
| Gestational age at targeted screening sonography (weeks) | 29 (25.86-32.57)                               | -                         |         |
| Gestational age at MRI scan (weeks)                 | 31.71 (30-33.86)                                   | 32.86 (31.43-35)          | .03     |
| BMI at MRI scan (kg/m²)                              | 24.9 ± 6 (16.8-48.4)                               | 23.2 (20.12-25.9)         | .25     |

*Note.* Data is presented as median (interquartile range) for continuous variables or as number (percent) for categorical variables.

*Abbreviations:* BMI, body mass index; COH, controlled ovarian hyperstimulation; IVF, in vitro fertilization; MRI, magnetic resonance imaging; US, ultrasonography.

---

**FIGURE 1** Two-dimension Ultrasonographic (A) and T2 MR image (B) of fetus at 34 gestational age suspected with retrognathia. The US raised a suspicion of micro/retrognathia without definitive diagnosis of the palate intact. The MR scan succeeded to depict additional findings including: cleft palate and glossoptosis. The cleft palate is demonstrated by high and posterior position of the tongue and disruptive line of the palate structure (white arrow)
three and was confirmed postnatally. Although the MRI agreed with the US diagnoses in two cases, diagnoses with both US and MRI turned out to be incorrect postnatally. In one case, the US diagnosis was rejected by MRI, hence that was incorrect as the neonate had bilateral cataract. In the comparison group, one fetus was referred for fetal MRI because of history of malformations in a previous pregnancy, with no findings in US screening survey. MRI diagnosed anophthalmia and was correct.

3.2.5 | Prenasal and frontal edema

Five cases with prenasal and frontal edema suspected on US were referred to fetal MRI. MRI confirmed that in two cases; however, only in one this was on both imaging methods as well as in the postnatal period. In the other case, the prenatal US and MRI diagnosis was incorrect on postnatal examination. In another case, the initial diagnosis on US was rejected by MRI, yet this was incorrect as the neonate had frontal edema. In two cases, the diagnosis at US was rejected by MRI, the latter being correct.

3.2.6 | Micrognathia/retrognathia

Five cases with micrognathia or retrognathia on US were referred for MRI. MRI confirmed this in three cases. This diagnosis on both imaging methods was only correct after birth in only two cases. In two cases, the US diagnosis was rejected by MRI, the latter interpretation being correct (Figure 3). One fetus was referred to fetal MRI for a macrocystic lymphatic malformation in the neck. Diagnosis of retrognathia was established in the neonate, although not suspected in both US and MRI. In the comparison group, one neonate was found to have isolated micrognathia at birth, although not suspected either on US or on MRI.

3.2.7 | Hypotelorism/hypertelorism

Of the five cases with hypo/hypertelorism on US, MRI confirmed the diagnoses in only one, and a diagnosis of semilobar holoprosencephaly was established. This was the correct postnatal diagnosis. In another case, the US diagnosis was rejected by MRI, yet this was incorrect: following termination because of other malformations and severe intrauterine growth restriction, hypertelorism was confirmed. In three cases, the US diagnosis was rightfully rejected by MRI.

3.2.8 | Ear structure anomalies

There were three cases with ear anomalies. MRI confirmed the diagnoses in two (microtia) and this was correct postnatally. In one case, MRI rejected the diagnosis at US and this was correct. Nonetheless,
three neonates in the study group were diagnosed with low set ears and one neonate was diagnosed with auditory canal stenosis; none of the diagnoses were suspected on US or MRI.

3.2.9 Forehead structure anomalies

Three cases with either frontal bossing or flattened forehead suspected on US were referred for fetal MRI. In all cases, MRI declined this diagnosis, an interpretation that was correct.

3.2.10 Cysts of the skull

Three cases with skull lesions/cysts suspected on US were referred to fetal MRI. MRI confirmed the diagnoses in two. In only one, this diagnosis established by both methods was correct. In the third case, diagnosis on US was rejected by MRI, and the MRI interpretation was correct.

3.2.11 Nuchal edema

In the three cases with nuchal edema, MRI confirmed the diagnoses in all three. Nonetheless, in only two, this was correct after birth. One neonate in the study group was born with nuchal edema which was not detected in both US and MRI.

3.2.12 Tracheoesophageal malformations

One case with suspected tracheoesophageal fistula and one case with suspected cervical mass obstructing the esophagus and trachea on US were referred to fetal MRI. In both, MRI declined the diagnosis, an interpretation which was correct.

3.2.13 Craniosynostosis

Two cases with craniosynostosis US were referred for fetal MRI. In one case MRI confirmed the diagnosis wrongfully. In one case MRI confirmed the diagnosis wrongfully. In the other case, MRI declined the diagnosis, which was correct. There were no neonates diagnosed with craniosynostosis.

3.2.14 Meningoencephalocele

There was one case with meningoencephalocele, which was confirmed by MRI, and this diagnosis was correct after birth.

Considering all cases in this study, there was complete agreement between US, MRI, and postnatal findings in 40 out of 73 suspected face or neck anomalies (54.8%). Twenty-four cervicofacial anomalies suspected on US were not confirmed on MRI, and in which the MRI interpretation was correct. Three anomalies interpreted correctly by US were not confirmed on MRI (cataract, frontal edema, and hypertelorism). In six cases, the diagnoses by both US and MRI were incorrect when correlated with the postnatal outcome (overdiagnosis). MRI provided additional information on four anomalies that were missed on US, especially in the case of cleft palate. There was one MRI overdiagnosis. Seven anomalies detected on pediatric examination were not recognized by both US and MRI (mostly ear structure anomalies). Out of the 85 anomalies (suspected by imaging or confirmed postnatally), confident diagnosis could be made by MRI in 68 (80%), not diagnosed in 10 (11.8%), and overdiagnosed in seven (8.2%). By US, confident diagnosis could be made in 44 anomalies (51.8%), not diagnosed in 11 (12.9%), and overdiagnosed in 30 (35.3%).

The comparisons between US and MRI, stratified by craniofacial anomalies, are presented in Table 2. In the majority of cases, US was in substantial to almost perfect agreement with MRI. US was in moderate agreement with MRI in the diagnosis of cleft palate and prenasal frontal edema (κ = 0.562 and κ = 0.56, respectively). US was in fair to no agreement with MRI in diagnosis of hypotelorism or hypertelorism (κ = 0.323), forehead structure anomalies, and tracheoesophageal malformations (κ = 0 for both comparisons).

Using postnatal diagnosis as the ground truth, Table 3 lists the sensitivity, specificity, and diagnostic accuracy for both imaging techniques in the detection of craniofacial anomalies. US and MRI yielded comparably high sensitivity for detecting most craniofacial anomalies. MRI performed better in detecting cleft palate than the US (100% vs. 70%), and US performed better in detecting prenasal frontal edema and hypotelorism or hypertelorism (100% vs. 50% for both comparisons). For detecting micrognathia or retrognathia, both imaging techniques have a sensitivity of 50%, and a relatively low sensitivity for detecting ear structure anomalies (33.3%). There was a high degree of specificity for both US and MRI in detecting all craniofacial anomalies. MRI performed better in detecting intact palate (97.9% vs. 93.7%).

4 DISCUSSION

Anomalies of the fetal head, face, and neck include a wide range of malformations, which produce various degrees of disfigurement and can result in severe functional impairment postnatally.1 It is essential to describe the complexity of the malformation and associated anomalies because of their neonatal implications. Thanks to improvement in prenatal diagnosis through US and MRI, the approach to fetuses with craniofacial anomalies has shifted from a diagnosis at birth to prenatal diagnosis.2 Prenatal diagnosis facilitates counselling by an oral and maxillofacial surgeon, and careful planning with a multidisciplinary team of the timing and mode of delivery, level of neonatal care required, and procedures that need to be considered.16-18

This study includes one of the largest published cohorts of craniofacial anomalies evaluated by fetal MRI. Our main objective was to assess the role of MRI as a complement to US in the diagnosis of craniofacial anomalies. As reflected by confident diagnosis and misdiagnosis rates obtained from our cohort, MRI was found valuable for prenatal diagnosis of craniofacial anomalies, and also provided additional information when compared with US. When stratified by the type of anomaly, in the majority of malformations, US was in substantial to almost perfect agreement with MRI. They were in moderate agreement regarding
TABLE 2  Agreement between ultrasonography and magnetic resonance imaging

| Face/Neck Anomaly               | Level of Agreement on Positive Findings in US | Level of Agreement on Negative Findings in US | Level of Disagreement on Positive Findings in US | Level of Disagreement on Negative Findings in US | Kappa | P value |
|--------------------------------|-----------------------------------------------|-----------------------------------------------|-----------------------------------------------|-----------------------------------------------|-------|---------|
| Cleft lip                      | 14 (13.2%)                                    | 91 (85.8%)                                    | 1 (0.9%)                                      | 0                                             | 0.96  | <.001   |
| Cleft palate                   | 8 (7.5%)                                      | 88 (83.0%)                                    | 6 (5.7%)                                      | 4 (3.8%)                                      | 0.562 | <.001   |
| Masses/cysts of the face or neck | 4 (3.8%)                                      | 100 (94.3%)                                   | 2 (1.9%)                                      | 0                                             | 0.791 | <.001   |
| Eye structure anomalies        | 5 (4.7%)                                      | 99 (93.4%)                                    | 1 (0.9%)                                      | 1 (0.9%)                                      | 0.823 | <.001   |
| Prenasal and frontal edema     | 2 (1.9%)                                      | 101 (95.3%)                                   | 3 (2.8%)                                      | 0                                             | 0.56  | .002    |
| Micrognathia/Retrognathia      | 3 (2.8%)                                      | 100 (94.3%)                                   | 2 (1.9%)                                      | 1 (0.9%)                                      | 0.652 | <.001   |
| Hypotelorism/Hypertelorism     | 1 (0.9%)                                      | 101 (95.3%)                                   | 4 (3.8%)                                      | 0                                             | 0.323 | .047    |
| Ear structure anomalies        | 2 (1.9%)                                      | 103 (97.2%)                                   | 1 (0.9%)                                      | 0                                             | 0.795 | .001    |
| Forehead structure anomalies   | 0                                             | 103 (97.2%)                                   | 3 (2.8%)                                      | 0                                             | NA    | NA      |
| Nuchal edema                   | 3 (2.8%)                                      | 103 (97.2%)                                   | 0                                             | 0                                             | 1     | <.001   |
| Cysts of the skull             | 2 (1.9%)                                      | 103 (97.2%)                                   | 1 (0.9%)                                      | 0                                             | 0.795 | .001    |
| Tracheoesophageal malformations | 0                                             | 104 (98.1%)                                   | 2 (1.9%)                                      | 0                                             | NA    | NA      |
| Craniosynostosis               | 1 (0.9%)                                      | 104 (98.1%)                                   | 1 (0.9%)                                      | 0                                             | 0.662 | .019    |
| Meningo-encephalocele          | 1 (0.9%)                                      | 105 (99.1%)                                   | 0                                             | 0                                             | 1     | .009    |

Abbreviations: MRI, magnetic resonance imaging; US, ultrasonography.

TABLE 3  Sensitivity, specificity, and diagnostic accuracy of ultrasonography and magnetic resonance imaging compared with postnatal diagnosis as the gold standard

| Face/Neck Anomaly                  | US Sensitivity | US Specificity | US Accuracy | MRI Sensitivity | MRI Specificity | MRI Accuracy |
|-----------------------------------|----------------|----------------|--------------|----------------|----------------|--------------|
| Cleft lip                         | 100%           | 98.9%          | 99%          | 100%           | 100%           | 100%         |
| Cleft palate                      | 70%            | 93.7%          | 91.4%        | 100%           | 97.9%          | 98.1%        |
| Masses/cysts of the face or neck  | 100%           | 98%            | 98.1%        | 100%           | 100%           | 100%         |
| Eye structure anomalies           | 80%            | 98%            | 97.2%        | 80%            | 98%            | 97.2%        |
| Prenasal and frontal edema        | 100%           | 97.1%          | 97.2%        | 90%            | 100%           | 97.1%        |
| Micrognathia/Retrognathia         | 50%            | 98%            | 96.2%        | 50%            | 99%            | 98.1%        |
| Hypotelorism/Hypertelorism        | 100%           | 97.1%          | 97.2%        | 50%            | 100%           | 99%          |
| Ear structure anomalies           | 33.3%          | 99%            | 95.3%        | 33.3%          | 100%           | 96.2%        |
| Forehead structure anomalies      | -              | 97.2%          | -            | -              | 100%           | -            |
| Nuchal edema                      | 66.7%          | 99%            | 98.1%        | 66.7%          | 99%            | 98.1%        |
| Skull cysts                       | 100%           | 98.1%          | 98.1%        | 100%           | 99%            | 99.1%        |

Abbreviation: MRI, magnetic resonance imaging; US, ultrasonography.

diagnosis of cleft palate and prenasal and frontal edema, and in fair to no agreement in diagnosis of hypotelorism or hypertelorism, forehead structure anomalies, and tracheoesophageal malformations.

Although US remains the method of choice for fetal screening,19 the utility of MRI for fetal evaluation has considerably increased in recent years for several reasons. First, MRI popularity has risen because of its safety and technological improvements.20 These include ultrafast sequences that significantly reduce motion artifacts, multiplanar capability, excellent soft tissue contrast, and a larger field of view.6,19,21,22 Second, MRI is less operator-dependent than US. The images can be stored for subsequent analysis or transmitted to a specialist for a second opinion.19 Third, MRI has an important role in situations in which US findings are impaired during pregnancy.23,24

US and MRI are complementary imaging techniques in the evaluation of fetal craniofacial anomalies.2 MRI has inherent soft tissue contrast and shows fetal anomalies, especially of the head and trunk, with
relative ease. It allows to confirm or refute equivocal sonographic findings and provides additional information about craniofacial anomalies and a possible underlying syndrome not detected by sonography, which may change the prognosis of the fetal anomaly and the management of the pregnancy and delivery.  

While many studies have demonstrated that MRI is a useful adjunct to US in the evaluation of complex fetal anomalies, the data regarding its efficacy in evaluation of craniofacial anomalies is limited. Moreover, most studies have compared findings at prenatal US with those at prenatal MRI, and no postnatal correlation was reported. When one attempts to evaluate the role of an imaging technique, the technique itself cannot be used as the end point. In the current study, available data on postnatal evaluation was a criterion for inclusion and was considered the reference. In this cohort, MRI provided a confident diagnoses of fetal craniofacial anomalies compared with US in many cases. Similar to other studies investigating the role of MRI as an adjunct to US in the evaluation of cleft lip and palate, we showed a sensitivity of MRI equal to 100% in the evaluation of cleft lip and palate. Sonographic detection of the palate was more difficult and yielded a sensitivity of 70% in detecting cleft palate. In our cohort, MRI successfully detected all cases of facial or neck cysts or tumors, and US over-diagnosed two cases of tumors. In a series of 18 tumors diagnosed prenatally, MRI diagnosis and histologic diagnosis were concordant in 73% of cases, and MRI findings changed the ultrasound diagnosis in 50% of cases.  

Several strengths and limitations of this study should be acknowledged. First, because of the scarcity of craniofacial anomalies and the limited years of MRI practice, our study is limited by the size of the study group and mainly the diversity of fetal anomalies. Although we have calculated the sensitivity, specificity, and accuracy of US and MRI in detecting specific craniofacial anomalies, caution should be exercised before determining the accuracy of MRI in the diagnosis of fetal craniofacial anomalies as some anomalies were diagnosed only in a few cases. Second, the study is retrospective in design, and the addition of a prospective validation cohort would be optimal. Third, selection bias is another limitation, as only fetuses with possible anomalies identified by skilled obstetric sonographers were referred for MRI. However, this is the population that probably benefits most from advanced imaging. Fourth, this is not a blinded comparison between two imaging techniques—the results of the US had been known to the radiologists when MRI was performed and interpreted. Although this knowledge was necessary for sequence selection and choosing planes of acquisition, this may induce a bias in favor of MRI. Nevertheless, it conforms to reality.  

Among the strengths of this study are the relatively large cohort of congenital craniofacial anomalies evaluated by MRI, postnatal evaluation considered as the gold-standard, the well-defined inclusion criteria for both the study and the comparison groups, and meticulous statistical methods. To overcome the limitations of our study and to generalize our conclusions, a multicenter prospective study should be conducted in order to further evaluate the contribution of fetal MRI to clinical management of congenital craniofacial anomalies.

## 5 CONCLUSION

In conclusion, thanks to a distinguished illustration of fetal face anatomy, multiplanar capabilities, large field of view, and high-contrast resolution, MRI has proven its complementary value to US in the prenatal evaluation of head, face, and neck anomalies. MRI provides valuable information that can alter patient counseling and care. We recommend that fetal MRI be conducted whenever craniofacial anomaly is suspected on prenatal US, and its use should further evolve with the increasing availability of fetal MRI.

## DISCLOSURE

The authors report no conflict of interest.

## FUNDING STATEMENT

No funding to declare.

## DATA STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

## ORCID

Roni Zemet [https://orcid.org/0000-0002-7746-3594](https://orcid.org/0000-0002-7746-3594)

## REFERENCES

1. Nuckolls GH, Shum L, Slavkin HC. Progress toward understanding craniofacial malformations. Cleft Palate Craniofac J. 1999;36(1):12-26.
2. MacArthur CJ. Prenatal diagnosis of fetal cervicofacial anomalies. Curr Opin Otolaryngol Head Neck Surg. 2012;20(6):482-490.
3. Frates MC, Kumar AJ, Benson CB, Ward VL, Temppany CM. Fetal anomalies: comparison of MR imaging and US for diagnosis. Radiology. 2004;232(2):398-404.
4. Wang G, Shan R, Zhao L, Zhu X, Zhang X. Fetal cleft lip with and without cleft palate: comparison between MR imaging and US for prenatal diagnosis. Eur J Radiol. 2011;79(3):437-442.
5. Zugazaga Cortazar A, Martin Martinez C. Usefulness of magnetic resonance imaging in the prenatal study of malformations of the face and neck. Radiolalicia. 2012;54(5):387-400.
6. Levine D, Hatabu H, Gaa J, Atkinson MW, Edelman RR. Fetal anatomy revealed with fast MR sequences. AJR. 1996;167:905-908.
7. Manganaro L, Tomei A, Fierro F, et al. Fetal MRI as a complement to US in the evaluation of cleft lip and palate. Radiol Med. 2011;116(7):1134-1148.
8. Pugash D, Brugger PC, Bettelheim D, Prayer D. Prenatal ultrasound and fetal MRI: the comparative value of each modality in prenatal diagnosis. Eur J Radiol. 2008;68(2):214-226.
9. Mailáth-Pokorny M, Words C, Krampl-Bettelheim E, Watzinger F, Brugger PC, Prayer D. What does magnetic resonance imaging add to the prenatal ultrasound diagnosis of facial clefts? Ultrasound Obstet Gynecol. 2010;36(4):445-451.
10. International Society of Ultrasound in Obstetrics & Gynecology Education Committee. Sonographic examination of the fetal central nervous system: guidelines for performing the “basic examination”
and the "fetal neurosonogram". Ultrasound Obstet Gynecol. 2007;29:109-116.

11. Salomon LJ, Garel C. Magnetic resonance imaging examination of the fetal brain. Ultrasound Obstet Gynecol. 2007;30(7):1019-1032.

12. Meyer R, Bar-Yosef O, Barzilay E, et al. Neurodevelopmental outcome of fetal isolated ventricular asymmetry without dilation; a cohort study. Ultrasound Obstet Gynecol. 2018 Oct;52(4):467-472.

13. Gat I, Hoffmann C, Shashar D, et al. Fetal brain MRI: novel classification and contribution to sonography. Ultraschall Med. 2016;37(2):176-184.

14. Tilea B, Alberti C, Adamsbaum C, et al. Cerebral biometry in fetal magnetic resonance imaging: new reference data. Ultrasound Obstet Gynecol. 2009;33(7):1019-1032.

15. Meyer R, Bar-Yosef O, Barzilay E, et al. Neurodevelopmental outcome of fetal isolated ventricular asymmetry without dilation; a cohort study. Ultrasound Obstet Gynecol. 2018 Oct;52(4):467-472.

16. Landis JR, Koch GG. The measurement of observer agreement for categorical data. Biometrics. 1977;33(1):159-174.

17. To WW. Prenatal diagnosis and assessment of facial clefts: where are we now? Hong Kong Med J. 2012;18(2):146-152.

18. Bergé SJ, Plath H, Van de Vondel PT, et al. Facial cleft lip and palate: sonographic diagnosis, chromosomal abnormalities, associated anomalies and postnatal outcome in 70 fetuses. Ultrasound Obstet Gynecol. 2001;18(5):422-431.

19. Sandrasegaran K, Lall C, Aisen AA, Rajesh A, Cohen MD. Fast fetal magnetic resonance imaging. J Comput Assist Tomogr. 2005;29(4):487-498.

20. Kanal E, Barkovich AJ, Bell C. et al; ACR Blue Ribbon Panel on MR Safety. ACR guidance document for safe MR practices. Am J Roentgenol. 2007;188(6):1437-1474.

21. Tsuchiya K, Katase S, Seki T, Mizutani Y, Hachiy J. Short communication: MR imaging of fetal brain abnormalities using a HASTE sequence. Br J Radiol. 1996;69(823):668-670.

22. Huppert BJ, Brandt KR, Ramin KD, King BF. Single-shot fast spin-echo MR imaging of the fetus: a pictorial essay. Radiographics. 1999;19 Spec No:S215-S227.

23. Perrone A, Savelli S, Maggi C, et al. Magnetic resonance imaging versus ultrasonography in fetal pathology. Radiol Med. 2008;113(2):225-241.

24. Prayer D, Brugger PC, Prayer L. Fetal MRI: techniques and protocols. Pediatr Radiol. 2004;34(9):693.

25. Mirsky DM, Shekdar KV, Bilaniuk LT. Fetal MRI: head and neck. Magn Reson Imaging Clin N Am. 2012;20(3):605-618.

26. Levine D, Barnes P, Madsen J, Abbott J, Mehta T, Edelman RR. Central nervous system abnormalities, assessed with prenatal magnetic resonance imaging. Obstet Gynecol. 1999;94(6):1011-1019.

27. Shimoto H, Kashima K, Yuasa Y, et al. MR imaging of non-CNS fetal abnormalities: a pictorial essay. Radiographics. 2000;20(5):1227-1243.

28. Hubbard AM, Adzick NS, Crombleholme TM, et al. Congenital chest lesions: diagnosis and characterization with prenatal MR imaging. Radiology. 1999;212(1):43-48.

29. Hubbard AM, Crombleholme TM, Adzick NS. Prenatal MRI evaluation of giant neck masses in preparation for the exit procedure. Am J Perinatol. 1998;15:253-257.

30. Roche CJ, Pilling DW, Walkinshaw SA, May PL. Extracranial vascular malformation: value of antenatal and postnatal MRI in management. Pediatr Radiol. 2001;31(10):706-708.

31. Blaicher W, Prayer D, Kuhle S, Deutinger J, Bernaschek G. Combined prenatal ultrasound and magnetic resonance imaging in two fetuses with suspected arachnoid cysts. Ultrasound Obstet Gynecol. 2001;18(2):166-168.

32. Nemec SF, Horcher E, Kasprian G, et al. Tumor disease and associated congenital abnormalities on prenatal MRI. Eur J Radiol. 2012;81(2):e115-e122.

How to cite this article: Zemet R, Amdur-Zilberfarb I, Shapira M, et al. Prenatal diagnosis of congenital head, face, and neck malformations—Is complementary fetal MRI of value? Prenatal Diagnosis. 2020;40:142–150. https://doi.org/10.1002/pd.5593