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ORIGINAL ARTICLE

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# Facial shape; height and width in the second and third trimester of pregnancy

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**ABSTRACT**

**Objectives:** The objective of this study is to calculate on 3D volumes obtained from 16 weeks' gestation normative data of facial height (FH), facial width (FW) and their ratio and to test these parameters in pathological cases.

**Methods:** In total, 228 volumes were analyzed: 207 from normal and 21 from pathological cases. After multiplanar correction to the exact midsagittal plane FH was measured from the nasion to the gnathion and FW between the most lateral points on the zygomatic arch.

**Results:** For both FH and FW the intra- and inter-observer intraclass correlation coefficient variability was 0.99 and the difference between paired measurements was less than 0.3 cm in 95% of the cases. FH increased from 1.48 to 5.08 cm (FH = −16.10 + 3.78 × log(GA), $R^2$: 0.93) and FW from 2.20 to 6.42 cm (FW: 4.19–17.18 × log(GA), $R^2$: 0.85). The ratio increased steadily until about 25 weeks and less thereafter (ratio: (1/GA) × 26.44 + 0.92, $R^2$: 0.23). In pathological cases 16.6% of measurements were outside the normal range.

**Conclusions:** This study provides normative data for FH and FW measurements and insight in normal facial growth after 16 weeks' gestation. FH exceeds FW growth especially before 25 weeks.

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Facial height; facial shape; facial width; fetal face; fetal ultrasound; second and third trimester; three-dimensional ultrasound

## Introduction

Prenatal recognition of abnormal fetal features can provide important information leading to suspicion and consequent diagnosis of chromosomal disorders and syndromes [1–3]. Several genetic disorders are accompanied by an aberrant facial shape. Trisomy 21 fetuses, for instance, tend to have a rounder face, whereas fetuses with velo-cardio-facial syndrome (22q11 deletion) have a longer face and fetuses with Crouzon syndrome a broader face [3]. These typical features are observed after birth, but little is known of the development of the facial shape throughout gestation in normal and abnormal cases.

Previous studies have investigated several sonographic facial features with two-dimensional (2D) ultrasound [4,5]. The more recent three-dimensional (3D) technique has shown to be of additional value in obstetric sonographic examinations, by enabling visualization of especially curved fetal structures with a high reproducibility and a success rate similar to 2D [6–9].

Although an experienced sonographer might suspect an abnormality based solely on subjective recognition, it is important to define objective measurements for accurate diagnostics, comparison, documentation and follow-up.

The aim of this study was to provide quantitative data on facial height (FH), facial width (FW) and facial shape (HF/FW ratio) obtained from 3D volumes in the second and third trimester of pregnancy. These normative data may define changes in shape of the growing fetal face. We also measured FH and FW in a number of pathological cases.

## Material and methods

The study was approved by the local ethics committee and all women gave written consent. FH and FW were measured in volumes collected cross-sectionally from healthy, low-risk, pregnant Caucasian women with a singleton and uncomplicated pregnancy. We determined gestational age according to the last menstrual

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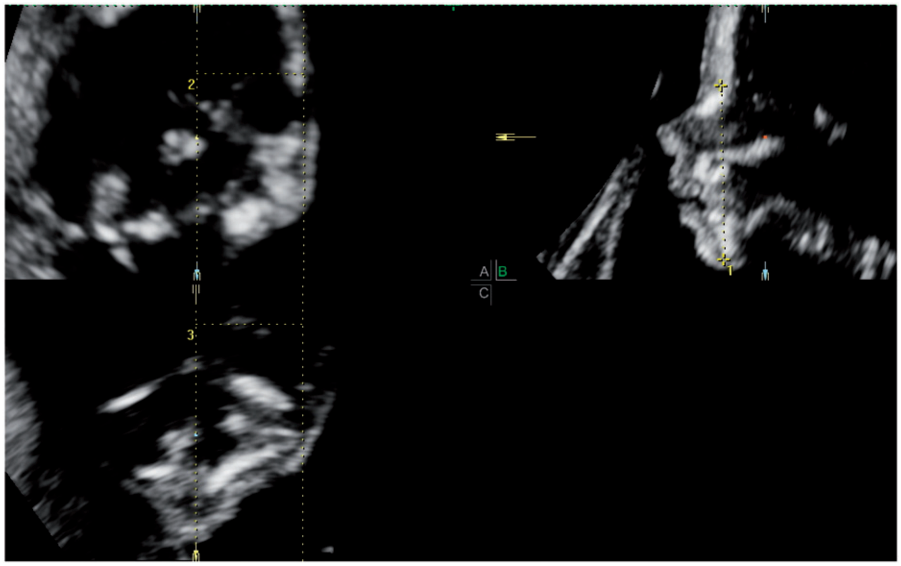


Figure 1. Multiplanar mode showing facial height measurement in Box B and facial width measurement in Boxes A and C.

period and by a first trimester dating scan. The second group consisted of stored volumes from 21 anomalous fetuses.

The examinations were carried out transabdominally, using a Voluson 730 Expert or an E8 ultrasound system (GE Medical Systems, Zipf, Austria). All ultrasound examinations were carried out by one experienced ultrasonographer (E. J. P.). When the fetus was facing the transducer with closed mouth, 3D volumes of the fetal head were acquired, starting at the midsagittal plane. An attempt was made to collect at least two volumes per fetus. The volumes were stored on removable digital media for subsequent analysis on 4D View software version 10.5 (GE Medical Systems, Zipf, Austria). Fetal gender was also assessed.

For each fetus, the volume with the clearest images was selected for further analysis. By use of the multiplanar mode (simultaneous display of the three perpendicular planes) in 4D View, the face was rotated to a coronal view in Box A, profile view in Box B and axial view in Box C and corrected to the exact midsagittal plane (Figure 1). The degrees of rotation on the fetal y-axis necessary to obtain this plane were noted. For standardized fetal head position the fetal profile line was turned vertically, thereby aligning the lower part of the forehead above the anterior part of the mandible [10]. The FH, visible in Box B, was defined as the distance between the nasion and the gnathion, with the nasion being the most anterior point at the intersection of the frontal and nasal bones and the gnathion the lowest point in the midline of the mandible. In case of a gap between the nasal and frontal bones in the midsagittal view, we defined the nasion landmark at the point of intersection between the lines tangential to both bones. FW, measured in Box C, was assessed in the axial planet below the orbits by measuring the distance between the exact midsagittal point and the most lateral point on the zygomatic arch on the best measurable side of the fetal face. The Box A was used to verify or the most lateral point on the zygomatic arch was identified (Figure 1). Based on previous sonographic investigations, suggesting that no significant right–left difference is to be expected, and taking into account the measurement is most reliable at the best visualized side, we calculated the FW by doubling the unilateral measurement [11]. We used the “distance between two lines” feature in 4D view to establish this distance (Figure 1). The facial shape was defined by the ratio of FH divided by FW. Volume contrast imaging was used where necessary to improve the image quality. Navigating with the multiplanar mode was frequently used in order to identify the exact landmarks. All measurements were performed by a single observer (A. G. B.).

Each measurement was given a subjective difficulty score (DS), ranging from 1 (low) to 3 (high), according to the time and effort it took to measure.

Measurement error was assessed by the intraclass correlation coefficient (ICC) and the Bland–Altman analysis [12] on randomly chosen paired volumes with at least 3 d between two assessments. For intero-bserver (second observer: E. J. P.) and intrao-bserver assessment 60 and 30 randomly selected cases were used, respectively. Ideally, a proper variability study is performed not only by remeasuring distances in stored volumes, but also by repeating the volume capturing and reacquiring the desired image. In our study, stored volumes were used; therefore, our results should be interpreted as assessing the measurement error of inter- and intra-observer measurements.

Data were analyzed using the statistical software SPSS version 19.0 for Windows (SPSS Inc, Chicago, IL) and Excel for Windows 2010. From all parameters (absolute measurements and ratios), the 5th, 50th and 95th percentiles were determined. The best fit polynomial line was used for constructing reference ranges. Correlations were determined by Pearson's correlation test. For gender differences, a *t*-test was performed. Differences in difficulty score were assessed by one-way ANOVA testing with an additional Bonferroni test. $p$ value $< .05$ was considered statistically significant.

## Results

The cross-sectional study group included 254 normal Caucasian fetuses. The gestational age ranged between 15 + 4 and 36 + 6 weeks (mean: 24 + 4 weeks). In 13 cases, no volume was stored because of unfavorable position of the fetus. Only high-quality volumes were selected, resulting in the inclusion of 207 cases. FH was measurable in 203 and FW in 151 cases. Rotation around the *y*-axis of a fetus applied to obtain the exact midsagittal profile varied between 2° and 39°. Our experience was that a volume taken with a starting plane between 10° and 20° around the *y*-axis of the fetus was most suitable for analyzing both the sagittal as the axial plane.

FH measurements increased from 1.48 to 5.08 cm, showing a logarithmic correlation with gestational age ($FH = -16.10 + 3.78 \times \log(GA)$, $R^2$: 0.93) (Figure 2). Gestational age and FH were highly correlated (0.96, $p$ value: $< .001$). No significant facial height difference was found between boys and girls (109 and 84 cases, respectively).

FW measurements also showed a logarithmic increase from 2.20 to 6.42 cm ($FW = 4.19 - 17.18 \times \log(GA)$, $R^2$: 0.85) with a significant correlation with gestational age (0.92, $p$ value: $< .001$) (Figure 3). A significant difference in FW between boys and girls (82 and 61 cases, respectively) was only found beyond 28 weeks of gestation, with boys having on average a 0.44 cm wider FW at a mean gestational age 30 + 3 weeks ($p$ value: 0.01).

The FH/FW ratio increased from 0.56 to 0.79. The measurement increased steadily until about 25 weeks and more moderately thereafter (mean: 0.75, SD: 0.07), (ratio: $(1/GA) \times 26.44 + 0.92$, $R^2$: 0.23) (Figure 4). A significant correlation between gestational age and the ratio was found (0.45, $p$ value: $< .001$).

The DS for measuring the FH was not influenced by the gestational age, whereas the measurement of FW became significantly more difficult with advancing gestation (at advanced GA a DS of three was more often scored than a DS of one; $p$ value: $< .01$) (Table 1).

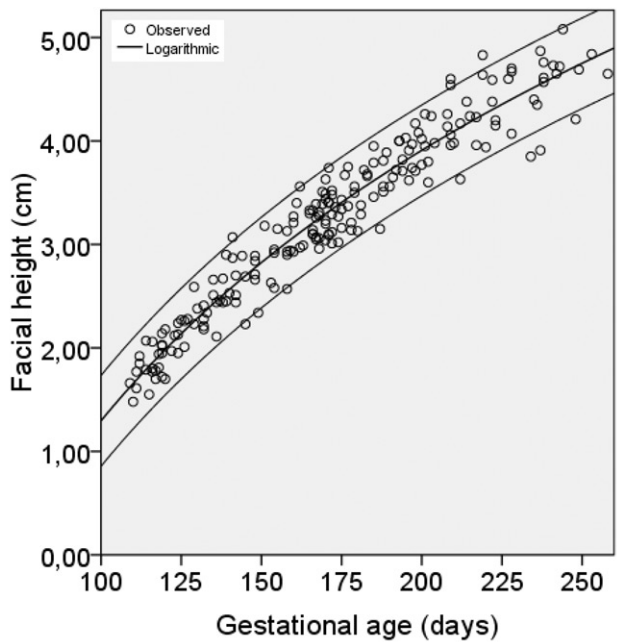


Figure 2. Scatterplot of facial height measurements against gestational age with reference curves (mean, 5th and 95th percentiles) derived from normal fetuses (facial height $= -16.10 + 3.78 \times \log(GA)$, $R^2$: 0.93).

The inter-observer ICC variability was 0.99 for both FH and FW measurements. The mean difference and 95% limit of agreements between paired inter-observer measurements were 0.005 (−0.21–0.22) and 0.023 (−0.29 to 0.34) cm for FH and FW, respectively. The intra-observer ICC variability was >0.99 for both FH and FW measurements. For paired measurements performed by one observer, the mean difference and 95% limits of agreement were 0.014 (−0.11–0.19) and −0.01 (−0.33 to 0.31) cm for FH and FW, respectively.

We examined a total of 21 pathological cases, of which 11 cases of trisomy 21, two cases of thanatophoric dysplasia type 1 – without cloverleaf skull, one case of thanatophoric dysplasia type 2 – with cloverleaf skull, three cases of bilateral cleft lip and one case of campomelic dysplasia, acrofacial dysostosis, trisomy 18 and Apert syndrome, respectively. We used the normal range values assessed in this study. A measurement between the 5th and the 95th percentile was defined as normal. The results are presented in Table 2. In three of the 11 cases with confirmed Down syndrome, FH or FW was outside the normal range. In two of the three cases with a facial cleft, the FH was below the normal range. In the case with campomelic dysplasia FH was below the normal range. In the fetus with Apert syndrome, the FH was at the upper limit

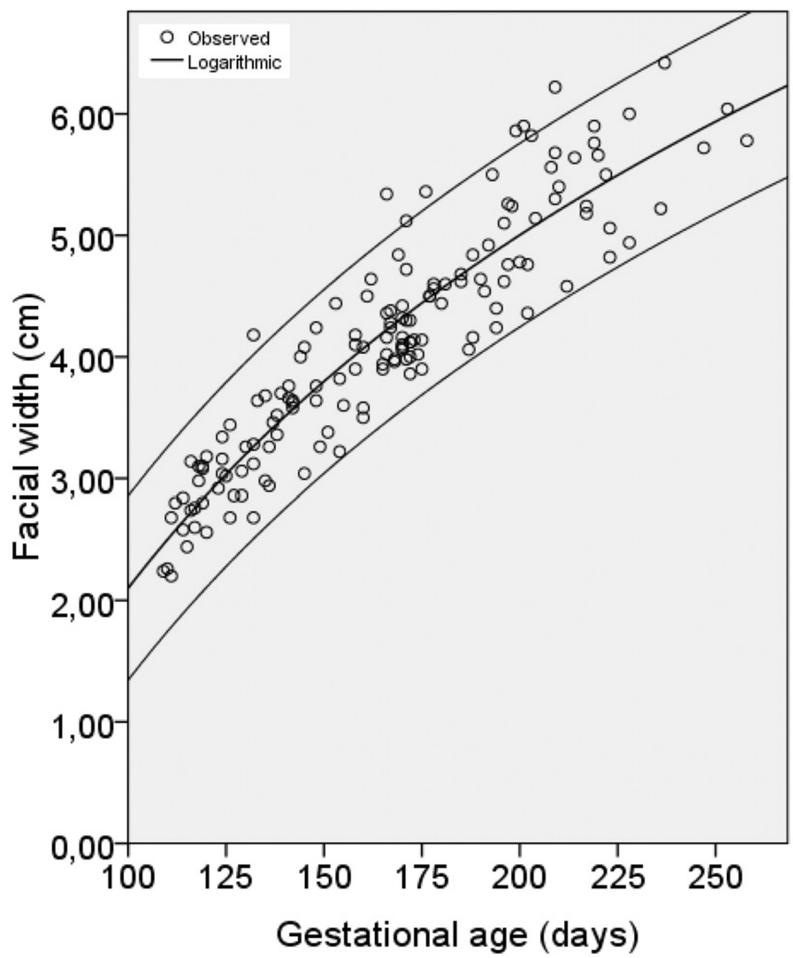


Figure 3. Scatterplot of facial width measurements against gestational age with reference curves (mean, 5th and 95th percentiles) derived from normal fetuses (facial width $=4.19-17.18\times\log(\mathrm{GA})$, $R^2$: 0.85).

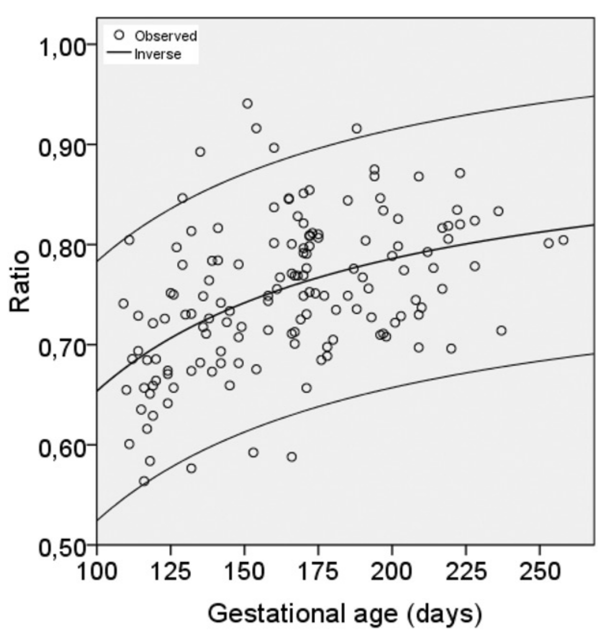


Figure 4. Scatterplot of the ratio (facial height divided by facial width) against gestational age with reference curves (mean, 5th and 95th percentiles) derived from normal fetuses (ratio: $(1/\mathrm{GA})\times 26.44+0.92$, $R^2$: 0.23).

Table 1. Difficulty score (DS) for facial height (FH) and facial width (FW) measurements with mean gestational age (days).

| | DS 1 | DS 2 | DS 3 | |
|---|---|---|---|---|
| FH | | | | |
| *N.* | 79 | 41 | 25 | |
| Mean GA (SD) | 165.72 (40.7) | 175.22 (37.5) | 185.44 (29.7) | *NS* |
| FW | | | | |
| *N.* | 35 | 25 | 38 | |
| Mean GA (SD) | 147.54 (24.3) | 167.72 (39.7) | 180.05 (37.1) | $p<.01$[a] |

[a]One-way ANOVA testing showed a significant difference in gestational age between DS 1 and 3; DS: difficulty score; FH: facial height; FW: facial width; *N*: number; GA: gestational age (days); SD: standard deviation; NS: not significant.

and the FW above the normal range. Overall 16.6% of the facial measurements in these fetuses fell outside the normal ranges.

## Discussion

In this study, we present second and third trimester nomograms for fetal facial height and width measured in 3D volumes corrected by multiplanar mode. For each fetus, a single volume was used for both

Table 2. Facial height (FH), facial width (FW) and the ratio (FH/FW) of 21 pathological fetuses.

| | Abnormality | Genetic confirmation | GA weeks (days) | FH | FW | Ratio |
|---|---|---|---|---|---|---|
| 1 | Trisomy 21 | Yes | 26 + 1 (183) | $4.17^{++}$ | 4.68 | 0.89 |
| 2 | Trisomy 21 | Yes | 30 + 2 (212) | 4.36 | 5.3 | 0.82 |
| 3 | Trisomy 21 | Yes | 22 + 1 (155) | 3.1 | 4.18 | 0.74 |
| 4 | Trisomy 21 | Yes | 30 + 4 (214) | 4.15 | 5.82 | 0.71 |
| 5 | Trisomy 21 | Yes | 31 + 2 (219) | 4.15 | 4.84 | 0.86 |
| 6 | Trisomy 21 | Yes | 21 + 2 (149) | $3.28^{++}$ | 4.06 | 0.81 |
| 7 | Trisomy 21 | Yes | 33 + 2 (233) | 4.26 | $4.72^{--}$ | 0.90 |
| 8 | Trisomy 21 | Yes | 17 + 4 (123) | 1.88 | 3.08 | 0.61 |
| 9 | Trisomy 21 | Yes | 24 + 4 (172) | $3.02^{-}$ | 4.12 | 0.73 |
| 10 | Trisomy 21 | Yes | 33 + 5 (236) | 4.55 | 5.74 | 0.79 |
| 11 | Trisomy 21 | Yes | 25 + 4 (179) | 3.58 | 4.2 | 0.85 |
| 12 | Thanatophoric dysplasia type 1 | Yes | 19 + 5 (138) | 2.43 | 3.56 | 0.68 |
| 13 | Thanatophoric dysplasia type 1 | Yes | 20 + 6 (146) | $2.38^{-}$ | 3.6 | 0.66 |
| 14 | Thanatophoric dysplasia type 2 | Yes | 21 + 2 (149) | 2.6 | 4 | 0.65 |
| 15 | Bilateral cleft lip | No | 25 + 3 (178) | $2.95^{--}$ | 4.22 | 0.70 |
| 16 | Bilateral cleft lip – Wolf Hirschorn Syndrome | Yes | 21 + 3 (150) | $2.34^{--}$ | 3.56 | 0.66 |
| 17 | Bilateral cleft lip | No | 27 + 1 (190) | 3.7 | 5.06 | 0.73 |
| 18 | Campomelic dysplasia | Yes | 20 + 5 (145) | $3.22^{--}$ | 4.22 | 0.76 |
| 18 | Acrofacial dysostosis | No | 32 + 0 (224) | 4.33 | 4.8 | 0.90 |
| 20 | Trisomy 18 | Yes | 20 + 4 (144) | 2.43 | 3.12 | 0.78 |
| 21 | Apert Syndrome | Yes | 32 + 1 (225) | $4.67^{+}$ | $6.4^{++}$ | 0.73 |

GA: gestational age in weeks (days); FH: facial height; FW: facial width; ratio: facial height/facial width; $++$: $>95$th percentile; $+$: normal range, near 95th percentile; $--$: $<5$th percentile; $-$: normal range, near 5th percentile.

measurements. A significant logarithmic increase in facial height (1.48–5.08 cm) and width (2.20–6.42 cm) was observed between 16 and 36 weeks' gestation. Facial shape defined by the ratio of height divided by width shows a steady increase with slight flattening in the third trimester.

Although the face is a complex structure not easily encompassed in simple measurements, these measurements give an overall basic impression of the facial shape.

Facial height and width were measured according to techniques described in the literature [13–18]. The amount of subcutaneous adipose tissue is known to increase in the third trimester fetus, and is strongly influenced by various individual maternal, paternal and fetal factors. To minimize these influences on our measurements, we used bony instead of soft tissue landmarks as opposed to measurements after birth.

As the face is a complex curved structure a standardized head position seems necessary to obtain reproducible measurements. After birth, the head can be placed in standard position using the Frankfurt horizontal plane [16]. This is not possible prenatally. To obtain a standard position in this study we, therefore, used the fetal profile line [10].

The progressive increase in FH/FW ratio indicates a relatively greater increment in facial height compared to width, especially before 25 weeks' gestation. This indicates that there is an elongation in the shape of the face. This growth pattern (faster growth in height than in width) seems to continue after birth, as illustrated by Farkas who noted a strong increase in FH/FW ratio of 19% (0.7–0.83) in the first 5 years of life [19].

The facial shape appears not related to gender, apart from the significantly larger width in boys beyond 28 weeks' gestation. Previous studies conducted by Merlob [20] and Chambers [21] report a lack of significant difference in male and female faces.

Measurement of the facial shape can be performed in a single 3D volume, with a low intra- and interobserver measurement error. Not surprisingly, measurements were more difficult to perform at more advanced gestational age; this was especially the case for FW measurements (Table 1). Later in gestation more shadow caused by bony structures, in combination with a more frequent unfavorable fetal position often hampered identification of the landmarks. The higher dropout rate for FW compared with FH measurements may be explained by the fact that volumes were taken from the profile view according to the original study design. However, during the study, a slight deviation from the exact midsagittal profile view seemed more favorable to identify landmarks necessary to measure FW. Furthermore, the increase in fat tissue seems to make the delineation of bony structures more difficult at advanced gestational ages especially effecting FW measurements. The multiplanar mode proved to be very useful in finding the most lateral point of the zygomatic arch, by comparing the FW distances on both coronal and axial view simultaneously (Figure 1).

The pathological group consisted of 21 cases with a variety of genetic and structural anomalies. Three of the 22 FH or FW measurements (14%) in the trisomy 21 group were above the 95th or below the 5th percentile. These findings confirm the conclusions of a study performed by Farkas, who analyzed 25 measurements in six craniofacial regions several facial features in children and adults with Down's syndrome. He found that more than half of the facial measurements were normal [22].

However, it is of note that 30% of the our measurements in the other pathological cases (six out of 20 values) were outside or close to the lower or upper limit of the norm (Table 2). Considering the limited number and diversity of pathological case it may well be possible that higher numbers of the same pathologies would show a trend. Of all pathological cases, the ratios were within the normal range, suggesting that calculation of ratios is prenatally less useful than FH or FW measurements alone.

Only a few previous studies have analyzed the normal facial growth *in utero*. Escobar [11] performed a morphometric analysis of the fetal craniofacies by 2D ultrasound at 16, 26 and 36 weeks of gestation. The growth rate for both height and width over the first 10-week period (16–26 weeks) exceeded that of the second period (26–36 weeks), which is consistent with our findings. More recently, Roelfsema assessed by 3D the changes of various facial features including the height, width and ratio [23]. In their publication, solely the ratio was displayed as a nomogram. In contrast to our finding, the authors found a steeper increase in width compared with height with advancing gestation, resulting in a slightly linear decrease in ratio with gestational age. The authors included soft tissue landmarks in the measurements, hampering comparison between the two studies.

In a postmortem study, Chambers assessed normal ranges of anthropometric facial height measurements in 260 s trimester autopsies (13–26 weeks' gestation) [21]. The chin-nasion measurements showed a linear increase throughout gestation.

In this study, only Caucasian, second and third trimester fetuses were included and 3D ultrasound was used. The findings in this study will not have direct clinical applications, but the nomograms constitute a basis for future research. In this study, only Caucasian, second and third trimester fetuses were included and 3D ultrasound was used; therefore, the results may not be applicable to non-Caucasian fetuses, the first trimester, and 2D images.

In conclusion, we have presented normative data on FH, FW and the FH/FW ratio of normal second and third trimester fetuses elucidating the dynamics of normal facial growth throughout gestation. More prospective studies are needed to establish a possible diagnostic role for these measurements in fetal dysmorphology.

## Disclosure statement

The authors report no conflict of interest

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