Mathematical assessment of foetal facial skeleton development

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Abstract

The goal of the study was to analyse statistically the survey of measurable parameters distinguishing human facial skeleton as well to construct mathematical model describing foetal facial skeleton selected features. The material consisted of 112 foetuses (44 females – 39.29% and 76 males – 60.71%) in the CRL: 83-245 mm, aged 4-7 months of foetal life. The whole of the examined material originated from the collection of the Department of Normal Anatomy, Medical University of Wroclaw. The study methods included: preparation, anthropological method, image acquisition with the use of digital camera as well as statistical methods. Symmetry and sexual dimorphism were evaluated. The following parameters were observed: head circumference – HC, bi parietal diameter – BPD, body mass, mandibular angle – Ang1, mental angle– Ang 2, mandibular body length – Lb, mandibular ramification length – Lra, mandibular body width – Wb, mandibular body width at the mandibular angle height – Wang, mandibular body width at the mandibular ramus height – Wra, coronoid process width – Wcp, mandibular condyle width – Wcon, mandibular height in medial line – A1, nasolabial groove height – A2, frontal bone height – A3, the distance between orbital edge and mandibular body – A4, nose length – A5, facial skeleton width on maxilla alveolar process level – S1, facial skeleton width on nasal cavity level – S2, facial skeleton width on orbital level – S3, facial skeleton height – W1. Female foetuses were significantly older than the male ones and asymmetry was not observed. Female foetuses facial skeletons (4th-6th month) are characteristic for mandible body Lb increased length, smaller mandibular angle Ang1 as well as the increase of Wang width and W1 height. The remaining parameters do not differ significantly in male foetuses. The growth rate of analysed parameters describing facial skeleton morphology was the biggest in 4th and 5th months. Logarithmic model seems to be the best to describe bone structures sizes dependence on foetal age.

Key words: foetus, development, metrology, jaw, facial skeleton.

Introduction

Ultrasound method belongs to basic examinations enabling detection of foetus developmental abnormalities. Ultrasound diagnosis of micrognathia is limited due to no objective measurements of foetal mandible. Otto and Platt [1] carried on cross-sectional surveys of 134 normal foetuses aged 14-39 weeks of foetal period. On the basis of squares regression analysis, foetal age based models were formed to predict mandibular length, biparietal size, head circumference and femoral bone length. Growth curves elaborated by the authors should help to diagnose foetal micrognathia.

Lee et al. [2] examined human mandible growth in 38 embryos and 111 foetuses with the use of histological and X-ray methods. The basic shape of mandibular development can be observed as early as in 7th week of foetal life. Starting from 14th week, mandibular condyle increase is distinguished in histologic and radiologic examinations. Malas et al. [3] described mandible increase basing on 161 foetuses without facial skeleton dimorphic features aged 9-40 weeks of foetal life. Neither asymmetry nor sexual dimorphism were found. Strong correlation of examined parameters and age was detected ($p < 0.001$). Mandible angle average value amounted to 122 ± 8° whereas mandible base average value was 65 ± 8°. Mandible growth was observed also by: Moss et al. [4], Low [5], Wilson et al. [6], Cortella et al. [7] as well as Żyśko et al. [8]. Woźniak et al. [9] described temporo-mandibular joint development in the period 7-12 weeks of foetal life. Germs of the joint component parts were observed as early as at the beginning of 7th week. In 9th and 10th weeks, the joint inferior cavity was formed and the superior one was observed in 11th week. Mahaczek-Kordowska [10] carried on the examinations on 75 human mandibles aged 4-9 months of foetal life with the use of preparational, radiological and sectional methods. Mandible vascularization derives from the inferior pridental artery as well as from the surrounding area and condylar process model resembled epiphysis. Inman et al. [11] observed frontal bone formation in 98 foetuses in 6-10 months of postnatal period. Similar studies were carried by Kvinsland [12] who found that the growth of the anterior lower base was more active than the one of the posterior cranial base. The ethmoidal
and sphenoidal parts of the anterior cranial base contribute equally towards the length increase.

Ricciardelli [13] described the review of the complex embryologic development and anatomic relationship of the cranial base. Sgouras et al. [14] studied skull base growth in craniosynostosis. Using three-dimensional visualisation techniques, 34 points of the skull base were identified on CT scans of 50 children with craniosynostosis of various types, aged 1 month to 5 years. The anterior fossa was overdeveloped in males and the body of the sphenoid showed moderate underdevelopment in the first 2 years in both sexes, the effect being more prominent in males. Ford [15] and Friede [16] also described normal development and growth of the human neurocranium and cranial base. Lee et al. [17] researched 64 normal Korean foetuses after 18. - 40. weeks of gestation. Roentgenograms were taken perpendicularly to the cranial base. The proportional growth of the anterior, middle and posterior cranial fossa could be assessed by the angle around the centre of the pituitary fossa as well as by the anterior, middle, and posterior cranial base angles. Kędzia et al. [18, 19] assessed foetal age on the basis of trunk selected parameters and head circumference. The study comprised 184 foetuses aged 10-30 weeks in the range CRL: 55-260 mm. No sexual dimorphism was observed. Analysed parameters increase was linear and the elicited results were compared with ultrasound outcome (literature data) and the increase curve was similar in character. Mathematical formula was elaborated to assess foetal age and its high correlation \( r = 0.811 \) with age proves its applicability in e.g. criminal investigations or foetal hypotrophy evaluation.

In their subsequent paper, on the material of 157 foetuses aged 10-29 weeks of foetal period (CRL: 55-260 mm), Kędzia et al. [20] examined craniometric parameters: orbits width and height, the distance between eye paramesial angles, frontal and sagittal angles length fibula. Long skulls were predominant and the increase of all analysed sizes in the period from 4th to 8th month had linear character. Orbits sizes symmetry was observed and sexual dimorphism was found. In male foetuses, orbits height, width and distance were significantly bigger. Skomra et al. [21] carried on cranial fossae metrological analysis in 13 foetuses aged 17-25 weeks of foetal period in the range CRL: 115-202 mm. Geometry and the changes taking place with age as well as fossae volume and symmetry were assessed. All parameters correlated with age. Cranial fossae volume revealed especially strong correlation and the dependence was of linear character. Due to mathematical formula, cranial fossae volume evaluation required foetal head length and mass only.

The goal of the study was to analyse statistically the results of measurable parameters survey as well as formation of mathematical formula to describe the increase of facial skeleton analysed parameters in foetal period.

**Material and methods**

The material consisted of 112 foetuses (44 females – 39.3% and 76 males – 60.7%) in the range CRL: 83-245 mm, aged: 4-7th months of foetal life. The whole of examined material originated from the collection of the Department of Normal Anatomy, Medical University of Wroclaw. Morphological age of foetuses was determined according to the dependence described by Scammon and Calkins [22]. The study methods included: preparation, anthropological method, image acquisition with digital camera and statistical methods (by Statistica program). Measurements of prepared bones were performed with the computer system Image J and Scion for Windows 98. The results of examined facial skeleton surveying were statistically analysed. All the specimens were photographed with millimetre scale which enabled pixels to millimetres rescaling. Image J and Scion for Windows 98 are computer programs reading linear sizes from digital photographs to within 0.01 mm. Own examinations revealed large applicability of computer systems: Scion for Windows 98 and Image J for metrological analysis during foetal period [23-27]. All sizes measurements were taken three times avoiding exposure of such a valuable foetal material to any damage. Symmetry and sexual dimorphism were examined. In every foetus,\( \text{CRL} \) (vertex – tuberale length), head circumference – \( \text{HC} \), \( \text{BPD} \) (biparietal diameter), body mass and vertex-plantare lengths were taken, as well as parameters: \( \text{Ang1} \) – mandible angle; \( \text{Ang2} \) – mental angle; \( \text{Lb} \) – mandible body length; \( \text{Lra} \) – mandible ramus length; \( \text{Wb} \) – mandible body width; \( \text{Wang} \) – mandible body width at mandibular angle height; \( \text{Wcp} \) – coronoid process width; \( \text{Wcoa} \) – mandibular condyle width; \( \text{A1} \) – mandibular height in mesial line; \( \text{A2} \) – nasolabial groove height; \( \text{A3} \) – frontal bone height; \( \text{A4} \) – the distance between orbit inferior edge and mandible body; \( \text{A5} \) – distance from the nose; \( \text{S1} \) – facial skeleton width at the level of maxillary alveolar process; \( \text{S2} \) facial skeleton width on the nasal cavity level; \( \text{S3} \) – facial skeleton width on the orbital level; \( \text{W1} \) – facial skeleton height [mm]. Fig. 1 presents basic parameters of mandible. Fig. 2 presents other measured parameters and visualizes the change in foetal and adult skulls proportions.
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\[
\text{Test statistic } t = 2.542; \quad P = 0.0124
\]

\[
\begin{array}{cccc}
26 & 28 & 30 & 32 \\
14 & 16 & 18 & 20 \\
\end{array}
\]

Fig. 1. Designations for mandibular parameters: \( \text{Ang}_1 \) – mandibular angle, \( \text{Lb} \) – mandibular body length, \( \text{ra} \) – mandibular ramus length, \( \text{Wb} \) – mandibular body width, \( \text{Wang} \) – mandibular body width at mandibular angle height, \( \text{Wra} \) – mandibular body width at mandibular ramus height, \( \text{Wcp} \) – coronoid process width, \( \text{Wcon} \) – mandibular condyle width

Fig. 2. Schematic difference in facial skeleton proportions in both foetal period and adult age. On the right – adult individual cranium. On the left – foetal facial skeleton with the following parameters: \( \text{A1} \) – mandible height in mesial line, \( \text{A2} \) – nasolabial groove height, \( \text{A3} \) – frontal bone height, \( \text{A4} \) – the distance between orbit inferior edge and mandible body; \( \text{A5} \) – nose length; \( \text{S1} \) – facial skeleton width on the level of maxilla alveolar process; \( \text{S2} \) – facial skeleton width on the level of nasal cavity; \( \text{S3} \) – facial skeleton width on the orbital level; \( \text{W1} \) – facial skeleton height

**Results**

Female foetuses were significantly older than male ones (Fig. 3) – by 2 weeks on average so statistically significant difference in somatic features was detected (v-pl, CRL, mass, HC, BP) – Fig. 4 and 5. Basic statistics (median and 95% CI for median as well as Wilcoxon’s test results for symmetric parameters) stand for lack of symmetry (Table 1). In the further correlation and regression analyses, the sizes of right and left sides were combined into one group. Table 2 presents regression formulas of analysed parameters in respect of foetus age (weeks) individually and collectively for both sexes. Table 2 includes the comparison result for these parameters average values at common age of 22 weeks (median age of examined foetuses).

Fig. 3. Age comparison graphs and independent samples t-test

Fig. 4. Length v-pl, CRL, body mass comparison graphs and Mann-Whitney test

Regression model of mandibular angle value change in the examined period is illustrated in figure 6. Statistically significant sexual dimorphism was observed for the following parameters (Fig. 7):
• mandibular angle Ang1 – smaller in female foetuses;
• Lb length – bigger in female foetuses (also after age influence elimination);
• Wang width – bigger in female fetuses;
• A4 distance – bigger in female fetuses;
• W1 facial skeleton height – bigger in female fetuses.

![Graphs showing HC and BP comparison](image)

**Fig. 5. HC (head circumference) and BP (bi-parietal size) comparison graphs and Mann-Whitney test**

**Table 1. Basic statistics – median (95% CI for the median)**

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Side</th>
<th>Wilcoxon test</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>left</td>
<td>right</td>
</tr>
<tr>
<td><strong>Ang1 [°] – angulus mandibulae</strong></td>
<td>110 (109 to 114)</td>
<td>110 (108 to 114)</td>
</tr>
<tr>
<td><strong>Lb [mm] – length of corpus mandibulae</strong></td>
<td>19.8 (19.0 to 21.4)</td>
<td>19.9 (18.9 to 21.7)</td>
</tr>
<tr>
<td><strong>Lra [mm] – length of ramus mandibulae</strong></td>
<td>8.9 (8.3 to 10.0)</td>
<td>9.2 (8.3 to 10.2)</td>
</tr>
<tr>
<td><strong>Wb [mm] – width of corpus mandibulae</strong></td>
<td>5.1 (4.8 to 5.6)</td>
<td>5.2 (4.8 to 5.7)</td>
</tr>
<tr>
<td><strong>Wang [mm] – width of angulus mandibulae</strong></td>
<td>6.3 (5.5 to 6.9)</td>
<td>6.0 (5.4 to 7.4)</td>
</tr>
<tr>
<td><strong>Wra [mm] – width of ramus mandibulae</strong></td>
<td>6.9 (5.8 to 8.0)</td>
<td>6.3 (5.4 to 7.8)</td>
</tr>
<tr>
<td><strong>Wcp [mm] – width of coronoideus processus</strong></td>
<td>3.0 (2.5 to 3.4)</td>
<td>2.8 (2.0 to 3.3)</td>
</tr>
<tr>
<td><strong>Wcon [mm] – width of condylus</strong></td>
<td>3.2 (2.7 to 3.6)</td>
<td>3.3 (2.5 to 3.6)</td>
</tr>
<tr>
<td><strong>A4 [mm] – the distance between orbit inferior edge and mandible body</strong></td>
<td>11.7 (10.7 to 12.5)</td>
<td>11.8 (10.6 to 12.6)</td>
</tr>
<tr>
<td><strong>Ang2 [°] – mental angle</strong></td>
<td>103.7 (98.4 to 115.2)</td>
<td>–</td>
</tr>
<tr>
<td><strong>A1 [mm] – mandibular height in mesial line</strong></td>
<td>5.2 (4.6 to 6.0)</td>
<td>–</td>
</tr>
<tr>
<td><strong>A2 [mm] – nasolabial groove height</strong></td>
<td>4.9 (4.5 to 5.2)</td>
<td>–</td>
</tr>
<tr>
<td><strong>A3 [mm] – frontal bone height</strong></td>
<td>29.9 (25.5 to 32.1)</td>
<td>–</td>
</tr>
<tr>
<td><strong>A5 [mm] – distance from the nose</strong></td>
<td>10.5 (9.5 to 11.5)</td>
<td>–</td>
</tr>
<tr>
<td><strong>S1 [mm] – facial skeleton width on the level of maxillary alveolar process</strong></td>
<td>25.2 (21.6 to 28.0)</td>
<td>–</td>
</tr>
<tr>
<td><strong>S2 [mm] – facial skeleton width on the nasal cavity level</strong></td>
<td>32.6 (28.6 to 35.6)</td>
<td>–</td>
</tr>
<tr>
<td><strong>S3 [mm] – facial skeleton width on the orbital level</strong></td>
<td>36.1 (32.4 to 39.4)</td>
<td>–</td>
</tr>
<tr>
<td><strong>W1 [mm] – facial skeleton height</strong></td>
<td>52.1 (46.8 to 57.9)</td>
<td>–</td>
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</tbody>
</table>
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Fig. 6. Regression model of mandibular angle value change in the examined period

Fig. 7. Parameters: mandible angle – ANG1, mandible body length – Lb, mandible body width on mandibular ramus height Wang, facial skeleton height – W1 and the distance between orbit inferior edge and mandibular body – A4, comparison graphs and Mann-Whitney test
Table 2. Regression models of analysed parameters in respect of foetus age (weeks) individually for males and females and collectively

<table>
<thead>
<tr>
<th>Y</th>
<th>Regression equation: $Y = a + b \times \text{Age (weeks)}$</th>
<th>F</th>
<th>M</th>
<th>Total</th>
<th>F vs. M $^*$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ang1</td>
<td>$Y = 61.6 + 37.45 \times \log(\text{Age})$</td>
<td>$Y = 56.9 + 44.42 \times \log(\text{Age})$</td>
<td>$Y = 93.2$</td>
<td>$P = 0.0117$</td>
<td></td>
</tr>
<tr>
<td>Ang2</td>
<td>$Y = 160.0$</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lb</td>
<td>$Y = -28.4 + 36.97 \times \log(\text{Age})$</td>
<td>$Y = -27.9 + 35.64 \times \log(\text{Age})$</td>
<td>$Y = 91.2$</td>
<td>$P = 0.0040$</td>
<td></td>
</tr>
<tr>
<td>Wb</td>
<td>$Y = -8.4 + 9.33 \times \log(\text{Age})$</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lra</td>
<td>$Y = 2.6 + 7.28 \times \log(\text{Age})$</td>
<td>$Y = -5.5 + 8.59 \times \log(\text{Age})$</td>
<td>$Y = 81.70$</td>
<td>$P = 0.0295$</td>
<td></td>
</tr>
<tr>
<td>Wra</td>
<td>$Y = 6.1 + 8.58 \times \log(\text{Age})$</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wcp</td>
<td>$Y = 6.8 + 9.33 \times \log(\text{Age})$</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wcon</td>
<td>$Y = 2.1 + 3.90 \times \log(\text{Age})$</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A1</td>
<td>$Y = 66.9 + 69.76 \times \log(\text{Age})$</td>
<td>$Y = 67.5 + 75.33 \times \log(\text{Age})$</td>
<td>$Y = 30.13$</td>
<td>$P = 0.3613$</td>
<td></td>
</tr>
<tr>
<td>A2</td>
<td>$Y = 87.7 + 92.66 \times \log(\text{Age})$</td>
<td>$Y = 67.3 + 103.6 \times \log(\text{Age})$</td>
<td>$Y = 17.24$</td>
<td>$P = 0.0331$</td>
<td></td>
</tr>
<tr>
<td>A3</td>
<td>$Y = -24.7 + 27.02 \times \log(\text{Age})$</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A4</td>
<td>$Y = -27.1 + 28.35 \times \log(\text{Age})$</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A5</td>
<td>$Y = -66.9 + 69.76 \times \log(\text{Age})$</td>
<td></td>
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</table>

*a comparison of parameters values adjusted to foetal age 22 Hbd. with Manna-Whitney’s test*

Discussion

After formation of the primary palate during the fifth and sixth weeks post conception, human facial morphology develops rapidly and by 10 weeks, the face has a typically human appearance. Facial skeleton development in foetal period was described by Diewert [28] who examined embryos and foetuses aged 7-10 weeks with CRL: 18-49 mm. Rapid directional growth of the primary cartilages is important in the development of normal human facial morphology and the interference with normal growth changes during this early critical period may produce irreversible effects on the face. Moyers et al. [29] described facial skeleton growth theory and Ferre et al. [30] examined biomechanical qualities of skull base and face. Levihn [31] carried on X-ray investigations of facial skeleton starting from 12th week of foetal life up to the delivery. The proportion of postnatal facial growth is the reverse of prenatal growth. At birth, the skull consists of forty-five bone elements separated by a cartilage or connective tissue. The ossification centres get formed in the second intrauterine month. At the age of 12 weeks, the embryo enters the foetal stage. There is usually a marked recession of the mandible, a pug nose, and a prominent bulging forehead. By the 12th, week the foetus has already tripled the length of the 8-week old embryo from 20 to 60 mm. The face then approaches human proportions. The most intensive growth rate during foetal life was observed in 4th and 5th lunar months. The growth rate during this period was greater than at any other time of life.

On the analysis of own material, the growth rate of parameters describing facial skeleton morphology was bigger in 4th and 5th months as well.

Conclusions

Female foetuses facial skeletons in prenatal period (4-6 months) are characteristic for increased mandible body length $Lb$, mandible smaller angle $Ang1$ as well as for bigger width $Wang$ and height $W1$. Other parameters do not differ significantly from male foetuses. Growth rate of the majority of sizes in 4th and 5th months is more intensive than this in 6th and 7th months. Logarithmic model seems to be the best adapted to describe the dependence between analyzed bone structures sizes and foetal age.
References


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