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ORIGINAL ARTICLE

FEATURES OF MORPHOGENESIS OF THE BONES OF THE HUMAN ORBIT

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ABSTRACT

The aim: To find out the sources of origin, the chronology of ossification, the peculiarities of age-related topographical and anatomical changes in the bones of the human orbit.

Materials and methods: The research was carried out on the specimens of 18 human embryos and prefetuses aged from 4th to 12th weeks of intrauterine development and 12 human fetuses aged from 4th to 9th months which were studied by microscopic examination and 3D reconstruction.

Results: The first signs of osteogenesis around the main nervous and visceral contents of the orbit rudiment are observed in 6-week-old embryos in the form of seven cartilaginous bone models. The first signs of ossification in the region of the orbit are found in the maxilla. During the 6th month of intrauterine development, intensive processes of ossification of the frontal, sphenoidal, ethmoidal bones and maxilla are noticeable. From the beginning of the fetal period of human ontogenesis, the ossification of bone rudiments that form the walls of the orbit continues. The processes of ossification of the structures of the sphenoidal bone continue, which leads to morphological transformations of the orbit in 5-month-old fetuses – it is separated from the sphenopalatine and infratemporal fossae by a bone layer, the optic canal is formed, and in 6-month-old fetuses, processes of ossification of the frontal, sphenoidal and ethmoidal bones and maxilla occur, Müller's muscle changes its structure to a fibrous one.

Conclusions: Critical periods of the orbit development are the 6th month of prenatal ontogenesis and the 8th month.

KEY WORDS: morphogenesis, human orbit, prenatal ontogenesis, critical periods

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INTRODUCTION

The study of the features of morphogenesis, the age-related dynamics of topographic-anatomical transformations and the anatomical variability of the bones of the human skull is an important task of modern morphology and an actual direction of anatomical and embryological research, the development of which contributes to the solving of an important medical and social problem – the improvement of methods of prevention, early diagnosis and effective correction of congenital and acquired human diseases, predicting the effectiveness and individualization of operative interventions in maxillofacial surgery, reducing infant mortality. The bones of the brain and facial parts of the skull form the orbit – an important region that includes the organ of vision and its auxiliary apparatus, the external muscles of the eye, blood vessels, nerves, and adipose tissue [1]. All these structures are in close syntopic connections, which affects the morphogenesis and topographic-anatomical changes of the orbit during the prenatal period of human development. Despite numerous scientific studies of the orbit, the organ of vision, and related structures, questions about the time and sequence of the appearance of bone sources that form the orbit, the chronology of their ossification, and critical periods of development are still pending [2, 3]. Elucidation of the sources of the bones of the human head, clarifying the sequence of their ossification will allow to create a morphological basis for the effective interpretation of fetal condition monitoring data [4, 5], will contribute to the early diagnosis of variants of the structure and possible defects in the development of the head, the organ of vision and adjacent structures, to the improvement of algorithms for the interpretation of diagnostic medical imaging data [6, 7, 8].

THE AIM

The aim of the research was to find out the sources of origin, the chronology of ossification, the peculiarities of age-related topographical and anatomical changes in the bones of the human orbit.

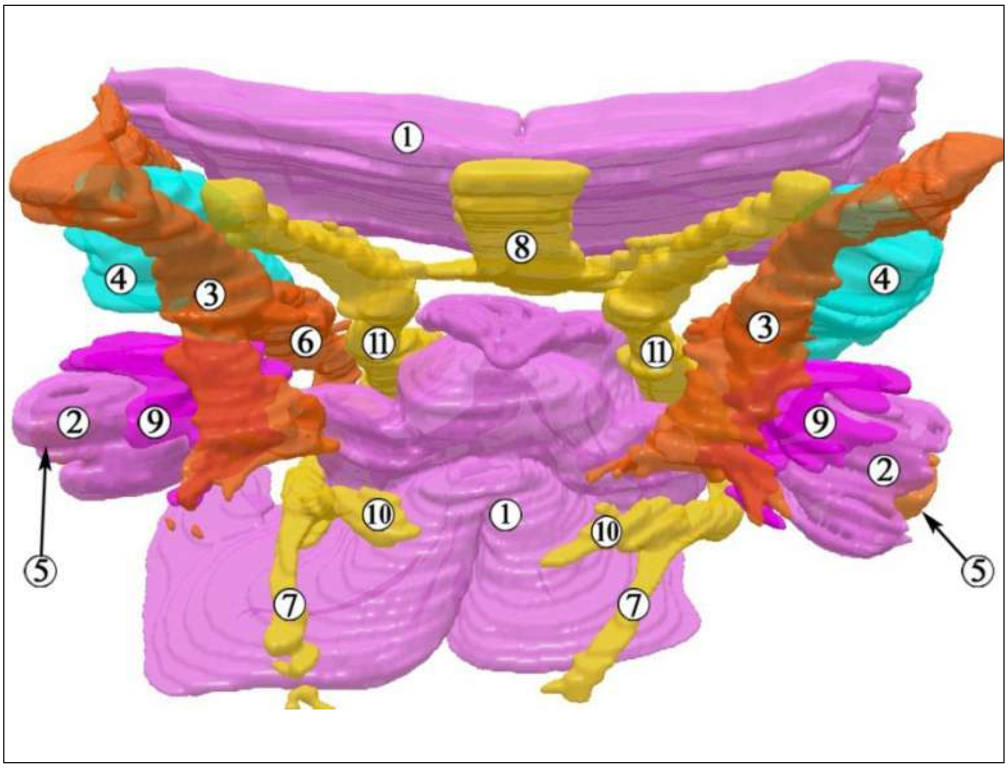

Fig. 1. 3D computer reconstruction of the structures of the head of a human embryo 8.0 mm PCoL (5th week of IUD). Front projection. Magnification: 30x. Signs:
1 – neuroectoderm of the brain; 2 – eye cup; 3 – internal carotid artery; 4 – trigeminal node; 5 – lens; 6 – posterior communicating artery; 7 – mandibular nerve; 8 – optic chiasm; 9 – mesenchymal condensation around the eye cups; 10 – maxillary nerve; 11 – ophthalmic nerve.

MATERIALS AND METHODS

The research was carried out on the specimens of 18 human embryos and prefetuses aged from 4th to 12th weeks of intrauterine development (IUD) (4.0-80.0 mm parietal-coccygeal length (PCoL)) and 12 human fetuses aged from 4th to 9th months of IUD (130.0-450.0 mm parietal-calcaneal length (PCaL)) using a complex of morphological research methods (anthropometry, morphometry, microscopy, macroscopy, 3D reconstruction of a series of histological sections and computer tomograms and statistical analysis).

The investigations were performed keeping to the major regulations of the Resolution of the First National Congress on Bioethics «General Ethic Principles of Experiments on Animals» (2001), ICH GCP (1996), the European Union Convention on Human Rights and Biomedicine (04.04.1997), and the European Convention for the Protection of Vertebrate Animals Used for Experimental and Other Scientific Purposes (18.03.1986), the Declaration of Helsinki on Ethical Principles for Medical Research Involving Human Subjects (1964-2008), EU Directives №609 (24.11.1986), the Orders of the Ministry of Health of Ukraine № 690 dated 23.09.2009, №944 dated 14.12.2009, № 616 dated 03.08.2012.

RESULTS

Our material revealed that the time of appearance of the sources of origin of structures of orbit is 4th weeks of IUD (embryos 4.0-5.0 mm PCoL). In this age period, for the first time, on separate histological sections and 3D-reconstructions of consecutive serial histological sections, mesenchymal condensation around the junction of the eye stalk with the forebrain is observed. The structures of the orbital region are located bilaterally, which is due to the mutual position of the rudiments of the eyeballs.

On the 5th week of IUD (embryos 6.0-8.0 mm PCoL), mesenchymal condensation surrounds the eye cups from all sides, which move from their lateral position (180°) to a more frontal one (Fig. 1), which can be considered the beginning the process of orbit frontalization.

In embryos 9.0-13.5 mm PCoL (6th week of IUD), morphological signs of the beginning of osteogenesis in the mesenchyme of the orbit area were found. 3D-reconstruction makes it possible to distinguish the rudiments of the bones of calvaria, the base of the skull and the face, in particular, the seven bones of the orbit. On the histological sections, the bone rudiments of orbit contain a grid of small zones of osteogenesis in its centers. Each bone sours consists of a thin mesenchymal capsule, which serves as a model for the morphogenesis of particular bones by both membranous and cartilaginous ossification. It should be noted that the maxilla is the first of the bones of the orbit to appear in the form of a single center of ossification above the dental plate at the place of source of the canine. Ossification zones increase in size and thus approach each other, demarcated by sutures.

The beginning of the pre-fetal period (the 7th week of IUD) is marked by intense rates of formation of the facial

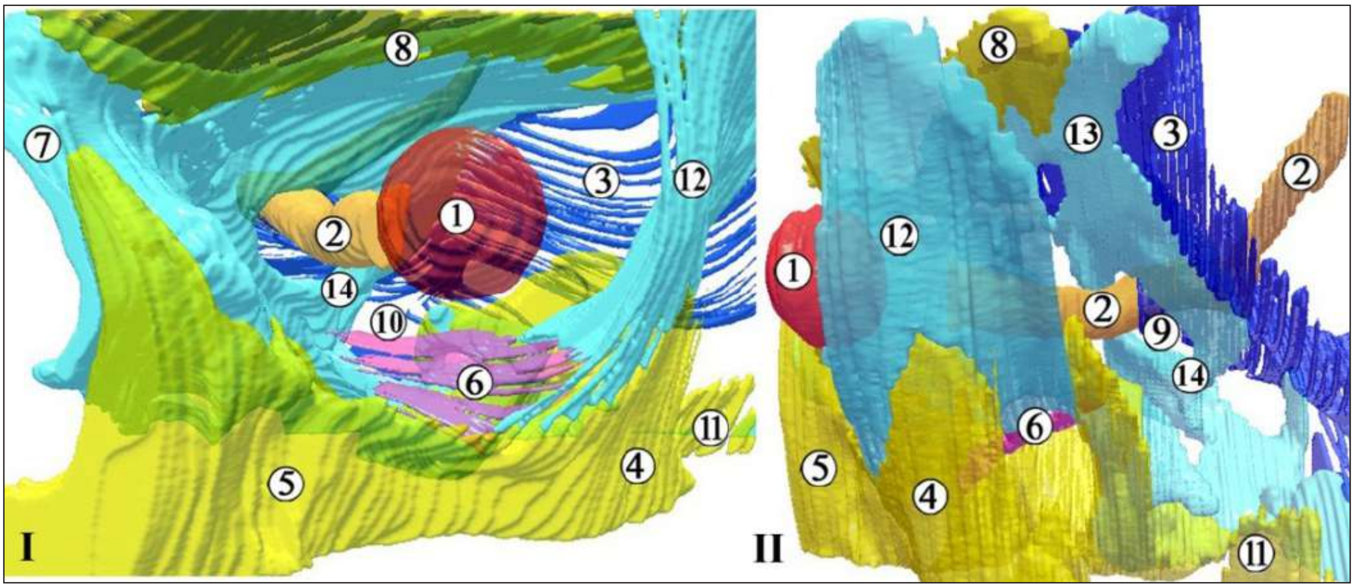

Fig. 2. 3D computer reconstruction of the structures of the left half of the head of the human fetus 22.0 mm PCoL (8th week of IUD). I – front projection, II – lateral projection. Magnification: 25x. Signs:
1 – lens; 2 – optic nerve; 3 – dura mater; 4 – zygomatic process of the maxilla; 5 – maxilla; 6 – Muller's orbital muscle; 7 – cartilaginous nasal capsule; 8 – frontal bone; 9 – optic canal; 10 – inferior orbital fissure; 11 – zygomatic process of the temporal bone; 12 – membranous lateral wall of the orbit; 13 – greater wing of the sphenoidal bone; 14 – lesser wing of the sphenoidal bone.

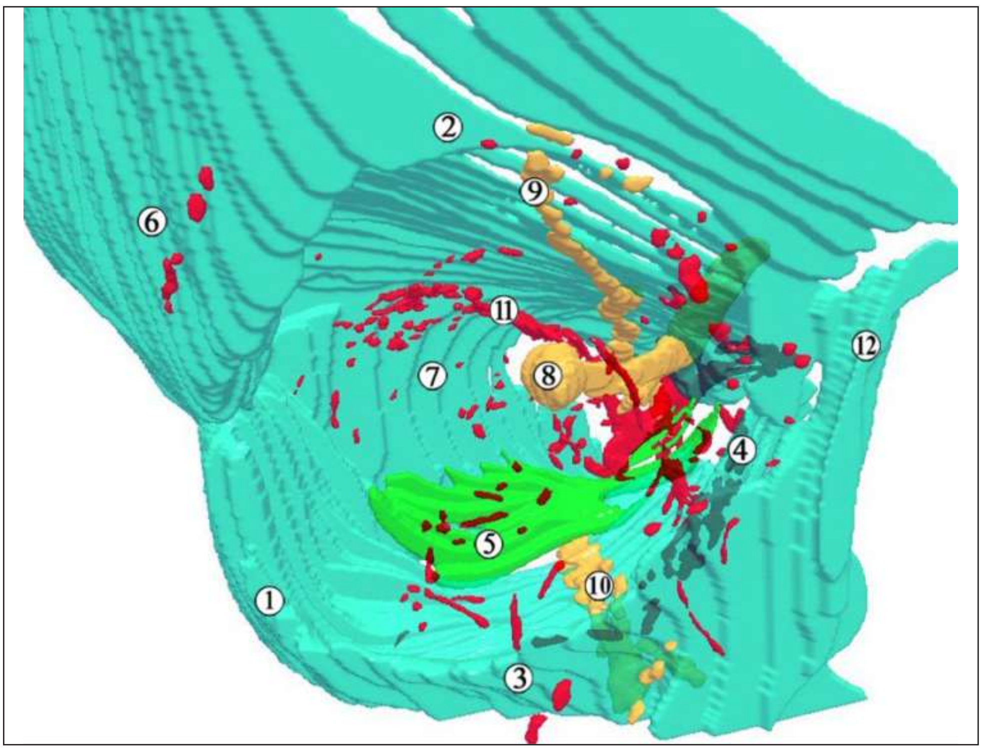

Fig. 3. 3D computer reconstruction of the right part of the head of the prefetus 50.0 mm PCoL (10th week of IUD). Front projection. Magnification: 25x. Signs:
1 – zygomatic bone; 2 – frontal bone; 3 – maxilla; 4 – lacrimal bone; 5 – Muller's orbital muscle; 6 – temporal surface of the greater wing of the sphenoidal bone; 7 – orbital surface of the greater wing of the sphenoidal bone; 8 – optic nerve; 9 – supraorbital nerve; 10 – infraorbital nerve; 11 – supra-orbital artery; 12 – nasal bone.

part of the head and the general growth of body parts. As a result, orbit quickly change their orientation to a more medial one while maintaining a still relatively significant interocular distance. By the end of the 8th week of IUD (prefetuses 24.0-28.0 mm PCoL), the shape of the face gradually acquires anthropomorphic features, but still with signs of hypertelorism. At the end of the 8th week of IUD, the membranous ossification of the frontal bone in the dorsal direction from the supraorbital edge, as well as the rudiments of the lesser wing of the sphenoidal bone in the form of a cartilaginous structure lateral to the optic nerve, are clearly visible (Fig. 2). Between the frontal bone and the lesser wing of the sphenoidal bone, a small cartilaginous structure is visible – sphenoido-ethmoidal cartilage. During the 8th week of IUD, osteogenesis begins through membra-

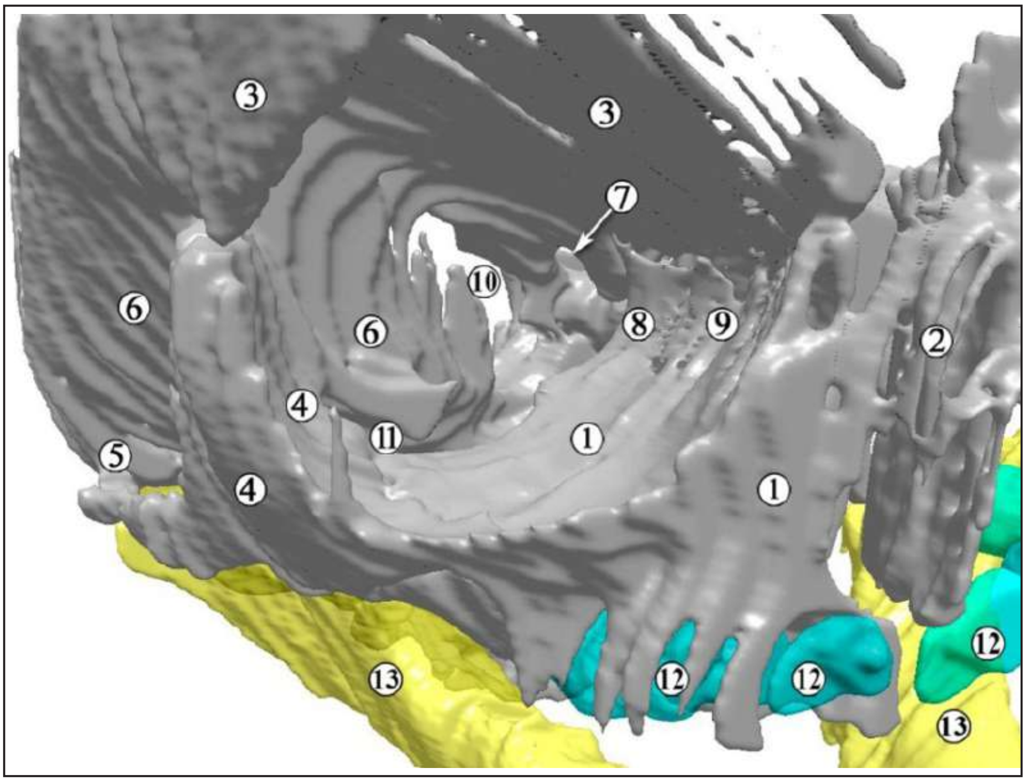

Fig. 4. 3D computer reconstruction of the right orbit of an 11-week-old human prefetus (60.0 mm PCoL). Front projection. Magnification: 25x. Signs:
1 – maxilla; 2 – nasal bone; 3 – frontal bone; 4 – zygomatic bone; 5 – zygomatic process of the temporal bone; 6 – greater wing of the sphenoidal bone; 7 – optic canal; 8 – ethmoidal bone; 9 – lacrimal bone; 10 – superior orbital fissure; 11 – inferior orbital fissure; 12 – teeth rudiments; 13 – mandible.

nous ossification of the zygomatic and palatine bones. An interesting fact is that the lower wall of the orbit is separated from the pterygopalatine fossa by Müller's orbital muscle.

Until the 10th week of IUD, the frontal reorientation of the orbit continues with a gradual slowing of this process. As a result, the interorbital distance decreases compared to the width of the face. Frontalization of the face contributes to the consolidation of the main facial rudiments (Fig. 3), therefore, on 3D-reconstructions, the face of the prefetuses acquires an anthropomorphic appearance.

In human prefetuses of the 10th week of IUD (42.0-52.0 mm PCoL), the ossification of orbital plate of the frontal bone begins already from the medial edge, as well as the bones of the medial wall of the orbit, in particular, the lacrimal bone, and the orbital plate of the greater wing of the sphenoidal bone. A wide spheno-frontal suture occupies most of the superior and lateral walls of the orbit. The peculiarity of this suture is that it is a chondromembranous connection between the frontal bone (membranous ossification) and the greater and lesser wings of the sphenoidal bone (cartilaginous ossification). The spheno-ethmoid cartilage regresses. We believe that this temporary structure provides a supporting framework for the superior wall of the orbit until the spheno-frontal suture is formed, similar to the role of the Müller muscle on the inferior wall of the orbit. Müller's orbital muscle has the appearance of a well-developed muscle plate that occupies more than half of the inferior wall of the orbit (see Fig. 3). The inferior orbital fissure at this stage of the IUD is very wide, since the membranous ossification of the bones that form it is not yet complete.

In the 11th week of IUD (prefetuses 55.0-65.0 mm PCoL), there is a linear increase in such morphometric indicators of orbit as width, height, depth and volume, but the dynamics of these changes are not proportional. Therefore, the shape of the contours of the external bony edges of the orbit (entrance to the orbit) changes from hameconchal (rectangular) at the beginning of the 11th week of IUD to hypsiconchal (rounded) (Fig. 4).

At the beginning of the fetal period (fetuses of the 4th month of IUD) the diameter of the orbit is 6.5±0.5 mm. The ossification of the rudiments of the bones that form the walls of the orbit continues – the unossified cartilaginous precursor of the ethmoidal bone gives rise to three outgrowths – the sources of the nasal concha. Müller's muscle separates the orbit from other regions, but the pterygopalatine fossa remains a continuation of the infratemporal fossa and the region around the sella turcica (Fig. 5).

The greater and lesser wings of the sphenoidal bone have only the lateral and medial centers of ossification, but ossification is more intense on the lateral edge of the lesser wings and on the medial edge of the greater wings of this bone. At the end of the 4th month of IUD, the medial center of ossification of the lesser wings of the sphenoidal bone becomes well defined, their size increases, due to which the connection of the infra-

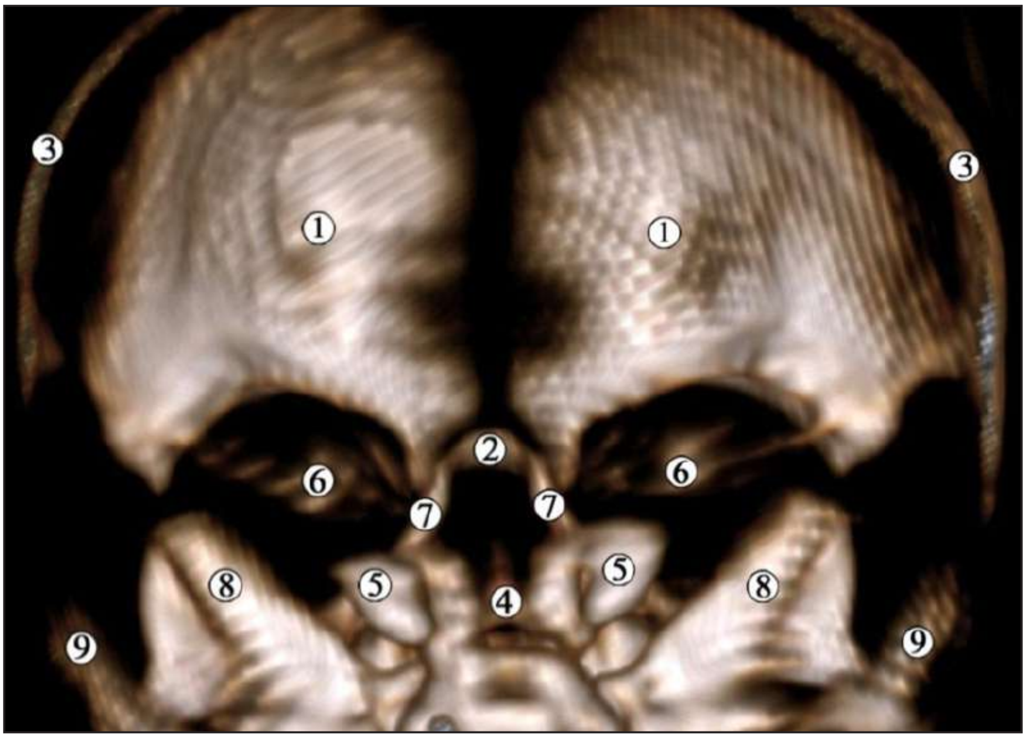

Fig. 5. Computer tomography of the head of a 4-month-old human fetus (180.0 mm PCaL). Posterior projection. Magnification: 3x. Signs:
1 – frontal bone; 2 – ethmoidal bone; 3 – parietal bone; 4 – the body of the sphenoidal bone; 5 – greater wing of the sphenoidal bone; 6 – lesser wing of the sphenoidal bone; 7 – frontal process of the maxilla; 8 – petrous part of the temporal bone; 9 – squamous part of the temporal bone.

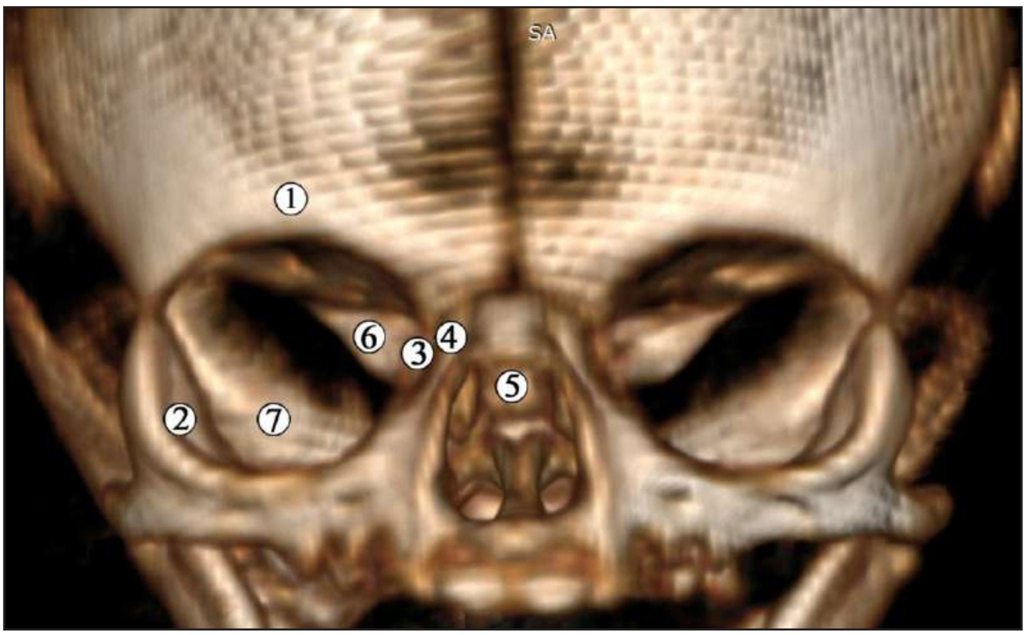

Fig. 6. Computed tomogram of the head of a 6-month-old human fetus 260.0 mm PCaL. Frontal projection. Magnification: 3x. Signs:
1 – frontal bone; 2 – zygomatic bone; 3 – ethmoidal bone; 4 – frontal process of the maxilla; 5 – body of the sphenoidal bone; 6 – lesser wing of the sphenoidal bone; 7 – greater wing of the sphenoidal bone.

temporal fossa with the orbit narrows, but the Müller muscle still delimits the orbit from the sphenopalatine-infratemporal complex.

From the middle of the 5th month of IUD, the diameter of the orbit is 9.7 mm. Due to the union of the medial and lateral centers of ossification, a definitive lesser wing of the sphenoidal bone is formed, which leads to the separation of the sphenopalatine and infratemporal fossae by a bone layer. Due to the development of the lesser wing of the sphenoidal bone, which surrounds the optic nerve, the definitive optic canal begins to form. The space between the greater and lesser wings of the sphenoidal bone is the beginning of the superior orbital fissure. At the end of the 5th month of IUD the orbit changes its shape to a more rounded, mesoconchal one. This is also facilitated by an increase in the height of the fetal orbit due to the development of the facial skeleton and an increase in the side wall of the nasal cavity (due to the development of the paranasal sinuses). Ossification centers appear in the ethmoidal bone and branches of the nasal concha.

On the 6th month of IUD, intensive ossification of the frontal, sphenoidal and ethmoidal bones and maxilla is visible on computer tomograms (Fig. 6). Müller's

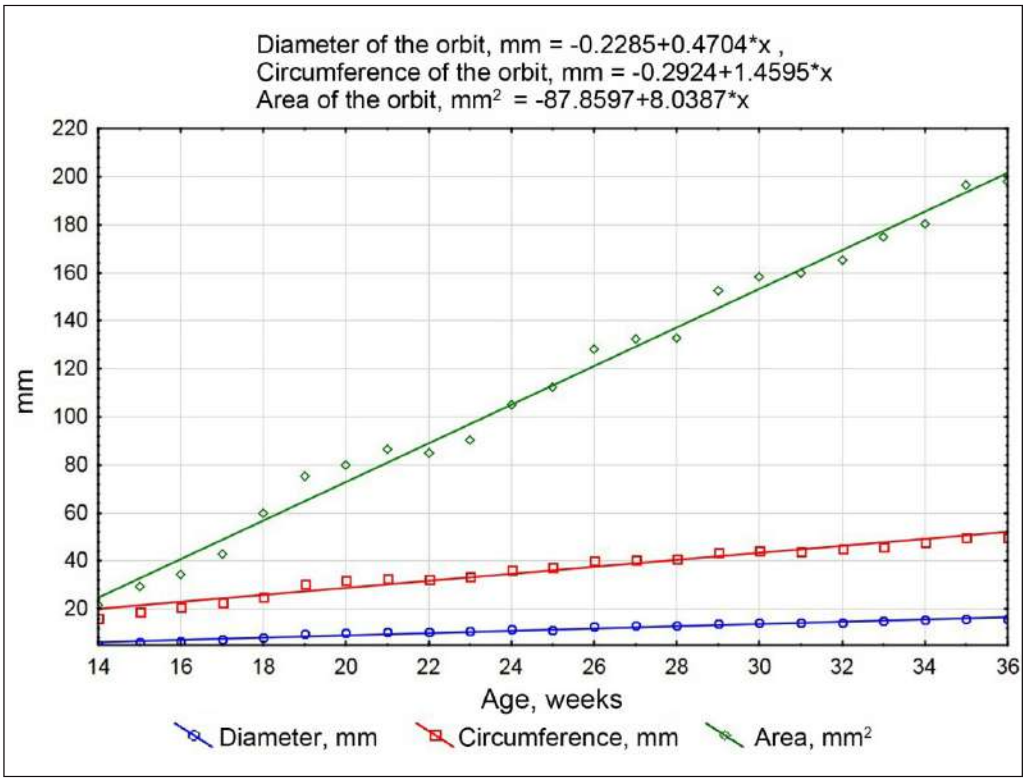

Fig. 7. Morphometric parameters of the orbit (diameter, circumference and area) in the dynamics of the fetal period of human development.

muscle decreases in size, and its smooth muscle fibers are replaced by bundles of collagen fibers.

At the end of the 6th month of IUD, the average diameter of the fetal orbit is 12.8 mm. The cartilaginous tissue of the rudiments of the bones of the orbit apex transforms into bone tissue, and the perichondrium transforms into periosteum with the formation of the tendon ring of Zinn around the optic canal and in the middle part of the superior orbital fissure.

At the end of the 8th month of IUD, the rudiment of the maxillary sinus appears. The structure of the lesser wing of the sphenoidal and frontal bones is approaching the definitive one. These bones come together and form a temporary orbito-spheno-frontal suture. The frontal bone and the greater wing of the sphenoidal bone also converge near the lateral wall of the orbit, forming a permanent lateral spheno-frontal suture. Ossification of the maxilla is progressing, although the ethmoidal bone is still partially ossified.

At the end of the 9th month of IUD, the average diameter of the orbit is 16.5 mm. As a result of the increase in the height of the orbit, it acquires a hypopsychonal form. At the end of the fetal period, the orbit should be considered still rudimentary, since it contains non-ossified connective tissue, primarily in the region of its apex, the ossification of the ethmoidal bone is not yet complete, and almost 50% of the inferior wall of the orbit is represented by Muller's muscle, which decreases in thickness, but not by area.

The analysis of the age dynamics of the morphometric parameters of the orbit during the fetal period of the IUD made it possible to establish the peculiarities of changes in its diameter, circumference and area. In general, these changes are characterized by linear growth (Fig. 7) with periods of slight intensification and deceleration, which are characterized by an uneven course of morphogenetic changes and topographic-anatomical relationships between the bones of the orbit, and therefore they can be critical in view of the appearance of variants of the structure and congenital malformations of the orbit.

Critical periods of the development of the orbit are the 6th month of IUD, during which there is an uneven growth rate of the horizontal size of the orbit relative to the vertical one, and its shape begins to return to the mesoconchal type, which is characteristic of prefetuses. These age-related changes in the shape and size of the orbit are caused by the growth of the eyeball, skull and face, which generally determines the shape of the orbit. Starting from the 8th month of IUD, the structure and topography of the orbit structures begin to acquire signs of a definitive state, the shape of the orbit is finally established, uniform growth rates of all parameters are determined, except for the growth of the circumference of the orbit at the end of the prenatal period of human ontogenesis.

DISCUSSION

Studies of the peculiarities of morphogenesis, structure, constitutional, sex-age anatomical variability of the bones of the human skull in the pre- and postnatal periods of human ontogenesis do not lose their relevance in connection with the tendency to increase the frequency of congenital malformations that cause severe perinatal pathology, difficulties in diagnosis, treatment and increase of childhood disability of human head structures [5, 6, 7]. Our study of the peculiarities of the morphogenesis of the orbit covers the entire prenatal period – from the origin of the orbit bone sources to the formation of its definitive structure, and the ossification processes continue even after birth.

It is known that the process of ossification of the human cartilaginous skull begins with almost 110 central centers of osteogenesis in the embryonic period of IUD [9]. These centers of ossification form 45 bones of the skull of a newborn, which begin to fuse in the postnatal period of development, and already in an adult their number is 22 bones. After the completion of their ossification, cartilaginous tissue is still preserved in some structures of the skull. Therefore, the formation of the skull continues until a person is 20 years old [1, 2, 6].

On the 8th week of IUD, membranous osteogenesis of the frontal bone occurs, which begins near the supraorbital bulge and spreads from front to back. Also, in this age period, the cartilaginous rudiment of the lesser wing of the sphenoidal bone lateral to the optic nerve is visualized. During the 8th week of IUD, the membranous ossification of the zygomatic and palatine bones is also observed, which generally agrees with the results of other researchers [3, 9]. It should be noted that the inferior wall of the orbit during this period of development is represented by Müller's orbital muscle, which delimits it from the pterygopalatine fossa. Muller's muscle is almost the only example of osteogenesis that begins with muscle tissue [10].

Ossification of the orbital plate of the frontal bone, which begins medially, as well as the lacrimal and orbital plates of the greater wing of the sphenoidal bone occurs in prefetuses of the 10th week of IUD. During this period of development, a lesser wing of the sphenoidal bone is formed, which gradually surrounds the optic nerve, and already at the beginning of the 5th month of IUD, the beginning of the optic canal is formed, and the space between the large and lesser wings turns into the superior orbital fissure. At the end of the 5th month of IUD, ossification centers also appear in the ethmoidal bone. In 6-month-old fetuses, the ossification of the frontal, sphenoidal and ethmoidal bones and maxilla accelerates. The Muller's muscle decreases in size and transforms into bundles of collagen fibers. We agree with Osanai H. et al. [10], who believe that the newly formed periosteum will eventually ossify with the formation of a bone plate along the inferior orbital fissure. At the end of the 8th month of IUD the beginning of the maxillary sinus appears.

The critical periods of the development of the orbit are the 6th month of IUD, during which there is an uneven growth rate of the horizontal size of the orbit relative to the vertical one, and its shape begins to return to the mesoconchal type, which is characteristic of prefetuses. These age-related changes in the shape and size of the orbit are due to the growth of the eyeball, skull and face, which generally determines the shape of the orbit and is consistent with the opinion of other researchers on this issue [11 - 15].

The morphometric regularities of changes in the parameters of the orbit during the fetal period that we have revealed can be useful for early diagnosis of variants of the structure and defects in the development of the orbit and head structures as a whole [16].

Until recently, the issues of typical and sexual variability of the shape and size of the calvaria, base, facial part of the skull and, in particular, the orbit, remained poorly studied. In our opinion, the research of the listed issues is relevant and dictated by the requests of anthropology, neurosurgery, maxillofacial surgery and forensic medicine. The detailing of morphological data on the structure of the bones of the calvaria, base and facial part of the skull is currently also needed to solve the problems of theoretical morphology, anthropology and bioengineering [5, 6, 7, 17].

CONCLUSIONS

1. The first signs of osteogenesis around the main nervous and visceral contents of the orbit rudiment are observed in 6-week-old embryos in the form of seven cartilaginous bone models. The first signs of ossification in the region of the orbit are found in the maxilla. During the 6th month of intrauterine development, intensive processes of ossification of the frontal, sphenoidal, ethmoidal bones and maxilla are noticeable.
2. At the end of the 8th month of intrauterine development due to the processes of ossification of the lesser wing of the sphenoidal and frontal bones, the orbit acquires definitive structural features.
3. From the beginning of the fetal period of human ontogenesis, the ossification of bone rudiments that form the walls of the orbit continues. The processes of ossification of the structures of the sphenoidal bone continue, which leads to morphological transformations of the orbit in 5-month-old fetuses – it is separated from the sphenopalatine and infratemporal fossae by a bone layer, the optic canal is formed, and in 6-month-old fetuses, processes of ossification

of the frontal, sphenoidal and ethmoidal bones and maxilla occur, Müller's muscle changes its structure to a fibrous one.

4. The analysis of the age-related dynamics of the morphometric parameters of the orbit during the fetal period of development made it possible to establish the peculiarities of changes in its diameter, circumference and area, which is expressed by mathematical functions:

Diameter of the orbit, mm = -0.2285+0.4704*x ,
Circumference of the orbit, mm = -0.2924+1.4595*x
Area of the orbit, mm^2 = -87.8597+8.0387*x ,
where x is the age of the human fetuses in weeks.

5. Critical periods of the orbit development are the 6th month of prenatal ontogenesis, during which there is an uneven growth rate of the horizontal size of the orbit relative to the vertical one, and its shape begins to return to the mesoconchal type, which is inherent in prefetuses, and the 8th month, during which the growth of all parameters of the orbit slows down due to intensive processes of organogenesis of its visceral structures.

REFERENCES

1. Gospe III.S.M., Bhatti M.T. Orbital anatomy. International Ophthalmology Clinics. 2018; 58(2): 5-23.
2. De Haan A.B., de Haan A.B., Willekens B., Klooster J., Los A.A., de Haan A.B., Simonsz H.J. The prenatal development of the human orbit. Strabismus. 2006; 14(1): 51-56.
3. Tawfik H.A., Dutton J.J. Embryologic and fetal development of the human orbit. Ophthalmic Plastic & Reconstructive Surgery. 2018; 34(5): 405-421.
4. Gujar S.K., Gandhi D. Congenital malformations of the orbit. Neuroimaging Clinics. 2011; 21(3): 585-602.
5. Burns N.S., Iyer R.S., Robinson A.J., Chapman T. Diagnostic imaging of fetal and pediatric orbital abnormalities. American Journal of Roentgenology. 2013; 201(6): W797-798.
6. Vachha B.A., Robson C.D. Imaging of pediatric orbital diseases. Neuroimaging Clinics. 2015; 25(3): 477-501.
7. Ondeck C.L., Pretorius D., McCaulley J., Kinori M., Maloney T., Hull A., Robbins S.L. Ultrasonographic prenatal imaging of fetal ocular and orbital abnormalities. Survey of ophthalmology. 2018; 63(6): 745-753.
8. Belle M., Godefroy D., Couly G., Malone S.A., Collier F., Giacobini P., Chédotal A. Tridimensional Visualization and Analysis of Early Human Development. Cell. 2017; 169(1): 161-173.
9. Zhang Q., Wang H., Udagawa J., Otani H. Morphological and morphometric study on sphenoid and basioccipital ossification in normal human fetuses. Congenit Anom (Kyoto). 2011; 51(3): 138-148.
10. Osanai H., Abe S., Rodríguez-Vázquez J., Verdugo-López S., Murakami G., Ohguro H. Human orbital muscle: a new point of view from the fetal development of extraocular connective tissues. Invest Ophthalmol Vis Sci. 2011; 52(3): 1501-1506.
11. Piot N., Barry F., Schlund M., Ferri J., Demondion X., Nicot R. 3D printing for orbital volume anatomical measurement. Surgical and Radiologic Anatomy. 2022; 44(7): 991-998.
12. Ten B., Esen K., Adanır S.S., Hamzaoğlu E.C., Çiçek F., Taghipour P., Talas D.Ü. Anatomic features of the cranial aperture of the optic canal in children: a radiologic study. Surgical and Radiologic Anatomy. 2021; 43(2): 187-199.
13. Vadgaonkar R., Rai R., Prabhu L.V., Rai A.R., Tonse M., Vani P.C. Morphometric study of the medial orbital wall emphasizing the ethmoidal foramina. Surgical and Radiologic Anatomy. 2015; 37(7): 809-813.
14. Grzonkowska M., Baumgart M., Badura M., Wiśniewski M., Szpinda M. Morphometric study of the primary ossification center of the frontal squama in the human fetus. Surgical and Radiologic Anatomy. 2020; 42(7): 733-740.
15. Hoyte D.A. Growth of the orbit. In Fundamentals of craniofacial growth. 2017; CRC Press: 225-256.
16. Escaravage Jr.G.K., Dutton J.J. Age-related changes in the pediatric human orbit on CT. Ophthalmic Plastic & Reconstructive Surgery. 2013; 29(3): 150-156.
17. Cornelius C.P., Mayer P., Ehrenfeld M., Metzger M.C. The orbits – Anatomical features in view of innovative surgical methods. Facial Plastic Surgery. 2014; 30(05): 487-508.

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