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Research Article

Development of the Orbit and Eyeball during the Fetal Period

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Abstract

Aim: We aimed to investigate the morphometric development of the orbit and eyeball in the fetal period.

Material and Methods: The present study was carried out on 136 fetal eyes (86 males, 50 females) obtained from 68 fetuses aged between 15-40 gestational weeks. In this study, the area, height, width, volume, depth, and circumference parameters of the orbit were measured, while the anteroposterior and transverse diameters, weight and volume parameters of the eyeball were measured. Also, the diameter at the place where the optic nerve enters the eyeball was measured.

Results: It was determined that all parameters increased during the trimesters and there was a statistically significant difference between the trimesters in all parameters. There was no statistically significant difference in all parameters in terms of gender. In the comparison of the right and left sides, orbital area ($p<0.011$), orbital circumference ($p<0.048$) and orbital width ($p<0.048$) were higher on the right side. There was no difference between the parties in any of the parameters related to the eyeball ($p>0.05$). However, the diameter of the optic nerve was higher on the left side ($p<0.001$).

Conclusion: The data we obtained will be very useful in evaluating the pregnancy follow-up by imaging methods such as ultrasonography or magnetic resonance, in the early diagnosis of malformations or diseases, and in planning the treatment.

Keywords: Optic nerve, imageJ, trimester, morphometry

INTRODUCTION

The cavity that contains and protects the eyeball and its auxiliary formations are called the orbit. The orbit is a prism-shaped structure that is formed by the joining various bones with the base at the front and top at the back to each other (1). The eyeball is positioned forward in the orbit to protect it and to provide good vision. Therefore, the eyeball occupies only 20% of the orbital volume. The space in the orbit not occupied by the eyeball is filled with veins and nerves supported by the orbital fat and connective tissue (2).

Ocular growth in fetuses can be determined by measuring different ocular structures at various stages of the fetal period. Data on the gestational ages of the eyeball and orbit are probably associated with fetal anthropometric growth. Therefore, knowledge of the normal anatomy of the eyeball and orbit can be helpful in the early diagnosis of fetal growth abnormalities and ophthalmic pathologies.

The wide usability and development of ultrasound technology have allowed for the prenatal measurements of the eyeball as well as the orbital parameters. Most of the studies in the literature have used prenatal ultrasonography (USG) for the measurement of the eyeball and orbital parameters (2-5). More recently, it has been used to obtain the normal growth parameters of fetal eyes with the magnetic resonance imaging (MRI) method (6). Data on ocular and orbital parameters from fetuses of

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different gestational ages are probably the most accurate morphometric and morphological assessment methods. Such morphometric studies may help understand the growth of the eyeball and orbit. Therefore, in the present study, we aimed to investigate the development of the orbit and eyeball in the fetal period.

MATERIAL AND METHOD

The present study was carried out on 136 fetal eyes (86 males, 50 females) obtained from 68 fetuses aged between 15-40 gestational weeks and not having external abnormality and pathology, which were provided by Maternity and Children Hospital by receiving permission from the families between 1996-2014 in the laboratory of Faculty of Medicine, Department of Anatomy. Approval for this study was obtained from the Ethics Committee of the Faculty of Medicine. The gestational week of the fetuses was determined according to the biparietal width, head circumference, femur length, and foot length. The fetuses in the fetal period were divided into the following three groups and evaluated: fetuses between 15-25 weeks were regarded to be in the 2nd trimester, fetuses between 26-37 weeks were regarded to be in the 3rd trimester, and fetuses between 38-40 weeks were regarded to be full term. 36 eyes from the 2nd trimester, 68 eyes from the 3rd trimester, and 32 eyes from the full term were included in the study.

The eyeball was removed from the orbit. The orbits were photographed with a ruler. The photographs were uploaded to the computer, and the orbital area, height, width, and circumference were measured in the ImageJ analytical software (National Institutes of Health, Bethesda, MD) (Figure 1).

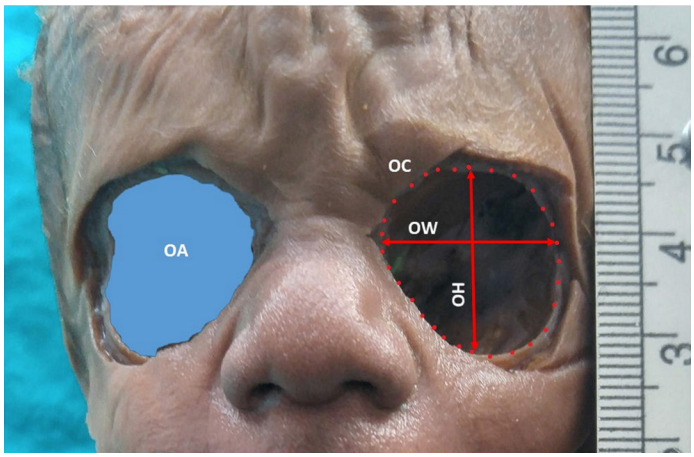

Figure 1. Measurement of orbital area, height, width and circumference. OA: Orbital area, OC: Orbital circumference, OW: Orbital width, OH: Orbital height

The mixture of Dentplus (organopolysiloxane dental impression material, EEC) mostly used by dentists and activator gel (EU) substances were applied to the orbital cavity to fill the orbital volume completely. This material was removed from the orbit after hardening and taking the exact shape of the orbit. The orbital depth (anteroposterior diameter) was measured using a digital caliper over the material that had taken the shape of the orbit (Figure 2). The orbital volume was determined by the water immersion method using the obtained orbital form.

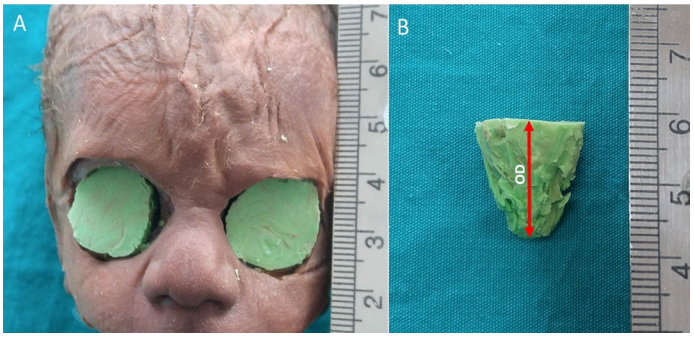

Figure 2. Orbital depth measurement. OD: Orbital depth

The tissues around the eyeball were cleaned. Physiological saline solution was injected into the eyeball with decreased intraocular fluid, and it was ensured that they reached a normal anatomical structure. The intraocular pressure was measured using a Schiotz Tonometer, and it was compared with normal values according to the scale. The intraocular pressure was measured at least three times, and the average value was calculated. Using the digital caliper, the diameter at the place where the optic nerve enters the eyeball, and the anteroposterior (AP) and transverse diameter of the eyeball (Figure 3) were measured. Using the Shimadzu AX 200 precision scales, the weight of the eyeball was measured, while the volume of the eyeball was measured by the water immersion method.

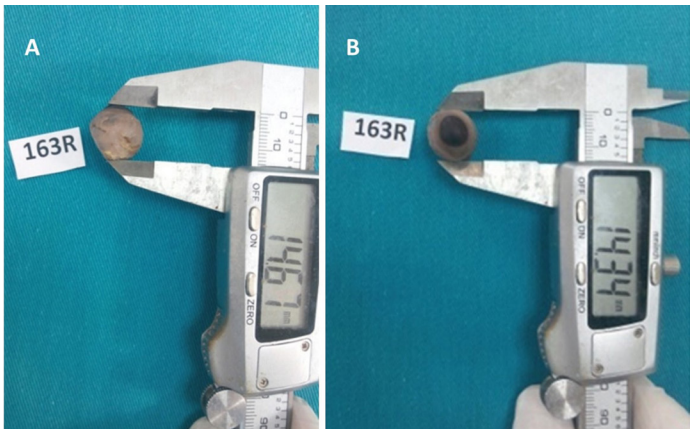

Figure 3. Diameters of the eyeball. A. Anteroposterior diameter of the eyeball B. Transverse diameter of the eyeball

Statistical Analysis

SPSS 17.0 statistical program was used in the analysis of the data. Since the data showed normal distribution, Independent Samples T-Test was used for pairwise comparisons (side and gender), and One-Way ANOVA test was used for trimester comparisons. In addition, the Pearson Correlation test was used in the correlation analysis. In the statistical analysis, the significance level of the data was taken as $p<0.05$.

RESULTS

Minimum, maximum, mean values and standard deviations

of all parameters evaluated in our study are presented in Table 1.

Table 1. Minimum, maximum, mean values and standard deviations of all parameters

	N	Minimum	Maximum	Mean	Standard Deviations
Orbital area (mm^2)	136	83.10	778.67	344.49	150.87
Orbital circumference (mm)	136	33.18	102.63	66.51	15.74
Orbital height (mm)	136	9.93	32.35	21.07	5.43
Orbital width (mm)	136	9.21	29.52	19.15	4.62
Orbital depth (mm)	136	12.17	31.41	20.57	4.08
Orbital volume (ml)	136	0.50	7.00	3.89	1.69
Eyeball antero-posterior diameter (mm)	136	6.14	21.00	14.38	2.95
Eyeball transverse diameter (mm)	136	6.92	19.30	13.92	2.37
Eyeball weight (gr)	136	0.28	3.15	1.58	0.67
Eyeball volume (ml)	136	0.10	3.00	1.48	0.71
Optic nerve diameter (mm)	136	0.94	4.31	2.57	0-.66

In the present study, the orbital area, orbital circumference, orbital width and height, orbital depth and volume were measured, and the mean and standard deviations of these parameters were calculated according to the trimesters, gender and sides (Table 2). It was determined that the orbit-related parameters increased during the trimesters and there was a statistically significant difference between the trimesters. There was no statistically significant difference in the orbit-related parameters in terms of gender. In the comparison of the right and left sides, there was no statistically significant difference in terms of the orbital height, orbital depth and orbital volume. However, it was determined that there was a statistically significant difference in the orbital area, orbital circumference and orbital width parameters between the right and left sides, and the right-side orbital values were higher (Table 2).

The AP diameter and the transverse diameter of the eyeball, the weight and volume of the eyeball, and the diameter at the point where the optic nerve enters the eyeball were measured, and the mean and standard deviations of these parameters were calculated according to the trimesters, gender and sides (Table 3). It was determined that the parameters related to the eyeball increased during the trimesters and there was a statistically significant difference between the trimesters. Upon evaluating the parameters related to the eyeball, no statistically significant difference was observed between the genders. When the right and left sides were compared, it was found that there was no statistically significant difference between the AP and transverse diameter of the eyeball, its weight and volume, but the diameter of the optic nerve was higher on the left side ($p<0.001$) (Table 3).

Table 2. Mean and standard deviation values of orbital parameters and their comparison by trimester, gender and sides

	N	Orbital Height (mm)	Orbital Width (mm)	Orbital Area (mm^2)	Orbital Circumference (mm)	Orbital Depth (mm)	Orbital Volume (ml)
^{2}nd trimester	36	15.37±4.21	14.04±3.42	192.72±122.64	49.52±13.72	16.95±3.25	2.08±1.31
^{3}rd trimester	68	21.98±4.03	19.74±3.04	353.21±107.54	68.25±10.51	20.44±2.75	4.01±1.01
Full term	32	25.57±3.59	23.66±2.77	496.70±79.50	81.94±6.33	24.92±3.08	5.64±1.14
P		<.001*	<.001*	<.001*	<.001*	<.001*	<.001*
Right	68	21.92±5.64	20.15±4.98	370.00±164.60	69.17±16.52	20.70±4.12	3.88±1.68
Left	68	20.23±5.11	18.15±4.02	318.98±132.09	63.85±14.56	20.44±4.07	3.90±1.71
P		0.069	0.011*	0.048*	0.048*	0.705	0.940
Male	86	21.14±5.64	18.99±4.88	341.94±157.32	65.99±16.68	20.25±4.11	3.81±1.68
Female	50	20.95±5.11	19.43±4.16	348.87±140.54	67.42±14.09	21.11±4.02	4.01±1.73
P		0.843	0.576	0.791	0.594	0.236	0.520

*p<0.05

Table 3. Mean and standard deviation values of eyeball parameters and their comparison by trimester, gender and sides

	N	Optic nerve Diameter (mm)	Eyeball Anteroposterior Diameter (mm)	Eyeball Transvers Diameter (mm)	Eyeball Weight (gr)	Eyeball Volume (ml)
[2]nd trimester	36	2.04±0.62	11.11±2.64	11.45±2.36	0.87±0.59	0.83±0.56
[3]rd trimester	68	2.61±0.53	15.06±1.95	14.49±1.48	1.65±0.40	1.51±0.48
Full term	32	3.09±0.51	16.60±1.78	15.49±1.77	2.22±0.47	2.14±0.61
P		<.001*	<.001*	<.001*	<.001*	<.001*
Right	68	2.37±.66	14.66±3.02	14.27±2.56	1.59±0.68	1.55±0.73
Left	68	2.77±.61	14.10±2.87	13.57±2.14	1.57±0.67	1.41±0.68
P		<.001*	0.267	0.083	0.840	0.242
Male	86	2.54±0.71	14.39±3.11	13.79±2.63	1.56±0.71	1.48±0.74
Female	50	2.63±0.59	14.36±2.67	14.13±1.86	1.62±0.62	1.47±0.65
P		0.433	0.941	0.382	0.588	0.937

*p<0.05

Table 4. The ratio of eyeball width to orbital width in trimester groups

	[2]nd trimester	[3]rd trimester	Full term
Eyeball transverse diameter (mm)	11.45±2.36	14.49±1.48	15.49±1.77
Orbital width (mm)	14.04±3.42	19.74±3.04	23.66±2.77
Eyeball transverse diameter (mm) / Orbital width (mm)	0.816	0.734	0.655

DISCUSSION

Investigating the development of the orbit, eyeball, and its attachments in the fetal period and revealing the standard parameters will guide the diagnosis and treatment of diseases in the studies to be conducted on this region. In previous studies on the orbit, the orbital depth, volume, circumference, area, width and height parameters have been evaluated in the fetal and adult periods.

In the study carried out on 70 fetuses aged 13-42 weeks, Haas et al. (7) measured the orbital depth and reported that the orbital depth increased linearly during the gestational age and there was no statistically significant difference in the parameters between the right and left sides. In the study conducted on 18 fetuses aged between 17-28 weeks, Tomasik et al. (8) indicated that the orbital depth increased together with gestational age. In our study, in parallel to previous studies, it was determined that the orbital depth increased during the gestational age (rweek=0.761, rtrimester=0.690) and there was no statistically significant difference between the right and left sides. Fitzhugh et al. (9) carried out a study on the orbital depth on 41 orbits of 21 adult skulls and determined no statistically significant difference in terms of gender. In our study, no statistically significant difference was also found in terms of the orbital depth between the genders. Hypotelorism, hypertelorism, masses, anophthalmia, microphthalmia, and cataract are some of the fetal orbital abnormalities (10). It is important to know the normal values of the orbit and to compare them with each other to identify malformations, to guide the diagnosis and treatment (11).

In order to calculate the orbital volume, Haas et al. (7) injected a silicone-like substance into the orbit and removed the substance after hardening and calculated the orbital volume. They used the weight formula while calculating the orbital volume. In the study, they found out that the orbital volume increased during the trimesters and there was no difference between the right and left sides. In a study carried out by Ji et al. (12), the orbital volume was determined by CT in 64 adults aged 18-50 years. Upon evaluating the orbital volume in terms of gender, the volume values were determined to be higher in males compared to females, but no difference was observed between the right and left sides. In our study, it was determined that the orbital volume increased during gestational age (rweek=0.818, rtrimester=0.747) and there was no statistically significant difference between the right and left sides and genders.

Goldstein et al. (4) measured the orbital circumference in the fetal period by USG in 14-36 week-old fetuses. Accordingly, they found a linear correlation between the orbital circumference and gestational week. Dilmen et al. (5) examined the relationship between bi-parietal diameter (BPD) and orbital diameters by USG in 15-40-week-old fetuses and accordingly found a linear growth between BPD and orbital diameters. Tomasik et al. (8) examined the orbital diameters in the fetal period and determined that the orbital diameters increased together with gestational age. Sukonpan et al. (13) measured the fetal orbital diameter, orbital circumference, and BPD by USG in 15-40 week-old fetuses during pregnancy and found

a strong linear correlation between the gestational week and the orbital diameter and circumference, and also they determined a strong growth relationship between the orbital diameter and BPD.

Fitzhugh et al. (9) measured the circumference of 41 orbits in 21 adult skulls and determined that the orbital circumference was wider in males. Ji et al. (12) measured the orbital circumference by CT in 64 adult individuals aged 18-50 years. Accordingly, the orbital circumference was higher in males compared to females, but no statistically significant difference was determined between the right and left sides. Seiji et al. (14) measured the orbital width, height, and circumference to investigate orbital asymmetry in 127 heads. The cases were examined by being divided into the following 4 groups: the 1st group was the intrauterine period, the 2nd group was the period between 0-2 years, the 3rd group was the period between 3-20 years, and the 4th group was the period between 21-76 years. Although the asymmetry ratios on the right and left sides were found to be higher in females, statistical significance was determined only in the 2nd group. Furthermore, these values were determined to be higher on the right side. In our study, it was determined that the orbital circumference increased during the trimesters (r=0.734) and there was a statistically significant difference between the trimesters. There was no statistically significant difference between the genders. However, a statistically significant difference was determined between the right and left sides and these values were found to be higher on the right side.

In a radiological study on the orbital area carried out on 30 fetuses aged between 18-41 weeks, Denis et al. (11) showed that there was a correlation between the orbital diameter and BPD. In the study on the orbital areas and diameter, Goldstein et al. (4) determined a linear correlation between gestational age and orbital areas and diameter. In a study conducted by USG, Dilmen et al. (5) indicated that there was a linear growth between BPD and orbital diameters. Tomasik et al. (8) demonstrated that the orbital diameter increased together with age. Sukonpan et al. (13) performed fetal orbital measurements by USG and determined a linear correlation between gestational age and the orbital area and diameter and between BPD and the orbital diameter. In the literature reviews we performed, no study on the orbital area in adults was encountered. In our study, it was determined that the orbital area increased during the trimesters (r=0.716) and there was a statistically significant difference between the trimesters. There was no statistically significant difference between the genders. A statistically significant difference was determined between the right and left sides and the orbital area on the right side was found to be larger (p=0.048).

Haas et al. (7) evaluated the orbital width and orbital height in fetuses. Accordingly, it was stated that the orbital width and height showed a linear increase with fetal age and there was no statistically significant difference between the right and left sides. Tomasik et al. (8) examined the orbital width and height in 17-28-week-old fetuses and demonstrated that both values increased with fetal age. Pommier (15) evaluated the orbital width and height in the fetal period by computed tomography (CT) and indicated that these distances could be used to determine fetal age. In a study conducted during the fetal period, Denis et al. (11) reported that there was no statistically significant difference between the genders in terms of orbital height. Fitzhugh et al. (9) measured the orbital width and height in adults and found these values to be higher in males compared to females. Ji et al. (12) measured the orbital width and height by CT. Accordingly, while there was no statistically significant difference in both parameters between the right and left sides, upon evaluating in terms of gender, the orbital width was determined to be higher in males compared to females and no statistically significant difference was found in the orbital height between genders.

According to our study, it was determined that the orbital width (r=0.743) and height (r=0.672) increased during the trimesters and there was a statistically significant difference between the trimesters. In our study, when the orbital width in the fetal period was compared between the right and left sides, it was found statistically significantly higher on the right side. However, no statistically significant difference was observed in the orbital height between the right and left sides.

In the MR study conducted on 17-39- week-old fetal eyes, Paquette et al. (16) demonstrated that the eyeball size plateaued at week 42. They determined no statistically significant difference in the eyeball width between the right and left sides. They also found that the size of all parameters in the fetuses doubled from the 17th week to the 22nd week. In a study carried out on 21-37 week-old fetuses, Ying et al. (17) determined the eyeball AP lengths and cranial AP lengths and found the ratios of these lengths. Accordingly, they found out the eyeball and cranial AP lengths increased during gestational age, but the cranial AP length was higher than the eyeball AP length from week 28 to full term. In our study, it was determined that the AP diameter (r=0.670), transverse diameter (r=0.613), weight (r=0.714) and volume (r=0.657) of the eyeball increased during the trimesters and there was no statistically significant difference between the trimesters. There was no statistically significant difference between the genders and the right and left sides. Moreover, when the width of the eyeball was proportioned to the orbital width in our study, this ratio was determined to decrease during gestational age, in other words, the orbit grew proportionally faster than the eyeball (Table 4).

In the literature reviews we performed, no study on the optic nerve diameter in the fetal period was encountered. Songur et al. (18) conducted research on 40 optic nerves in 20 adult cadavers and determined the width, height, and length of the optic nerve. In their study, the width and height of the optic nerve were measured from the midpoint of the nerve and no statistically significant difference was found between the right and left sides. In our study, the diameter

at the point where the optic nerve enters the eyeball was measured, and it was determined that the optic nerve diameter increased during the trimesters (r=0.562) and there was a statistically significant difference between the trimesters. There was no statistically significant difference in terms of gender. In the comparison between the right and left sides, a statistically significant difference was determined and the left optic nerve diameter was found to be greater.

We believe that the data we obtained will be very useful in evaluating the pregnancy follow-up by imaging methods such as USG or MR, in the early diagnosis of malformations or diseases, and planning the treatment. Our study is a basic study conducted in a large series on the orbit and eyeball during the fetal period, and the obtained data will shed light on clinical studies and studies to be conducted in the future on the eyeball and orbit.

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Conflict of Interest: *The authors declare that they have no competing interest.*

Ethical approval: *Approval was obtained from the Süleyman Demirel University Faculty of Medicine Ethics Committee for this study (Date: 11.19.2014, Decision Number: 185).*

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