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Original Article

Position and Dimension of the Inner Ear in Midterm Fetuses

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BACKGROUND: This study aimed to see the change in the area covered by the inner ear (IE) in the petrous bone with gestational age, and to determine the growth dynamics of inner ear structures such as the cochlea and semicircular canals.

METHODS: Twenty temporal bones of 10 fetal cadavers (5 males and 5 females) aged 23.50 ± 2.94 weeks were included in the study.

RESULTS: The petrous ridge length (PRL), the inner ear length (IEL), the thickness of bone on the cochlea, the distance of the rearmost part of the superior semicircular canal to the most posterior border of the petrous ridge, and the distance of the frontmost part of the cochlea to the most anterior border of the petrous ridge were measured as 23.97 ± 4.21 mm, 13.31 ± 1.45 mm, 1.26 ± 0.20 mm, 6.86 ± 1.97 mm, and 3.85 ± 0.93 mm, respectively. The ratio of the IEL to the PRL decreased despite of proportional increase in these parameters with age. This finding shows that the growth dynamics of the IE are slower than that of petrous bone, and thus the area ratio covered by the inner ear in the petrous bone decreased with age. The size of the cochlea and the angles between the semicircular canals did not correlate with gestational age. However, the semicircular canals (their thicknesses and inner surface areas) attain adult size between 21 and 24 weeks.

CONCLUSION: Our findings may be useful for otologists to see the relation of the IE with the petrous bone. Our numeric dataset may form a basis of prenatal radiologic investigations.

KEYWORDS: Cochlea, fetus, inner ear, lateral semicircular canal, petrous bone, posterior semicircular canal, superior semicircular canal

INTRODUCTION

The inner ear (IE) is located in the petrous bone and contains sense organs of balance (the semicircular canals and vestibule) and of hearing (the cochlea).[1] Jackler et al[2] observed that on radiological images (e.g., computed tomography [CT]) of patients (98 ears of 63 cases) with congenital IE malformations, the involvement rates of the cochlea, semicircular canals, and vestibular aqueduct were 76%, 39%, and 32%, respectively. The sum of the percentages exceeded 100% in their work because more than 1 structure of the IE was involved in some subjects.[2,3] They divided patients with congenital IE abnormalities into 2 main groups: cases with an abnormal cochlea and cases with a normal cochlea.[2] They classified the former group as follows: a) complete labyrinthine aplasia (no IE development), b) cochlear aplasia (no cochlea), c) cochlear hypoplasia (small cochlear bud), d) incomplete

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partition (a minor cochlea with an incomplete septum or without an interscalar septum), and e) common cavity (the space formed by the vestibule and cochlea but no containing internal architecture).[2] They classified the latter group as follows: a) enlarged vestibular aqueduct and b) lateral semicircular canal (LSC) and vestibule dysplasia (a short LSC with an enlarged vestibule).[2] If the source of congenital IE abnormalities is only the membranous labyrinth, the patient's radiological images will likely show normal IE morphology, but if the abnormality originates from the osseous labyrinth (the otic capsule), it will be possible to see signs of change in IE morphology (e.g., small cochlea) on radiologic views.[3]

Technological progressions in instruments of imaging like CT, magnetic resonance imaging (MRI), or ultrasonography (US), and growing anatomical information (e.g., dimensions or positions of IE's structures) help clinicians to diagnose ear abnormalities in utero.[4-10] Most of the above-mentioned abnormalities regarding IE occur in the first trimester of pregnancy on account of an interruption, which is a result of a teratogenic exposure or inborn genetic error.[2,3] Moreover, most researchers prove that IE's structures including the cochlea, LSC, superior semicircular canal (SSC), and posterior semicircular canal (PSC) reach an adult-equivalent morphology (including their dimensions, angulations, and shapes) in the early second trimester.[1,4,8-10] In these contexts, some researchers used US to examine the cochlea or semicircular canals for diagnosing IE anomalies as early as possible.[4,6] Leibovitz et al[4] achieved a practicable prenatal cochlear imaging in the early second trimester. In older fetuses, the petrous bone's ossification results in acoustic shadowing that hides the cochlea during US.[4,11] In light of all this information, a novel dissection study conducted on IE's structures in midterm fetuses may be important for clinicians to observe changes in their morphologies with age, to see the relation of these structures with the petrous ridge, and to create a numeric dataset for forming a basis of prenatal US and MRI investigations. We aimed to examine IE morphology in second trimester fetuses to improve the present information regarding anatomical properties of the prenatal IE.

METHODS

Ethical Statement

This fetal cadaveric examination was confirmed by the Institution's Ethics Committee of Mersin University (approval no.: 2022/463, date: July 6, 2022).

Study Population

Twenty temporal bones of 10 fetal cadavers fixed with 10% formalin were included in the investigation. Five of them were male and 5 were female. The mean age of the fetuses was calculated as 23.50 ± 2.94 weeks of gestation (range: 19-28 weeks).

MAIN POINTS

- This study examines the IE by removing it en bloc.
- This study investigates the localization of IE within the petrous bone.
- The study findings may form a basis for intrauterine ultrasonography and magnetic resonance imaging examinations.

Inclusion and Exclusion Criteria

The examination was carried out in the Institution's anatomy laboratory. Fetuses were added to the Institution's anatomy inventory between 2000 and 2005. Considering the limited information available on these fetal samples (parental data, presence of any genetic or syndromic diseases, the causes of death, their age, etc.), all second trimester fetuses were included in the study population. Prenatal radiologic data after the 18th week of gestation provide more accurate outcomes in detecting congenital malformations.[12] Thus, the starting age of the fetuses in this study was determined as the 19th week. Afterwards, 1 fetus was included in the work for each week until the end of the second trimester (i.e., 28th week). Exclusion criteria were as follows: a) fetuses with any visible deformity such as cleft lip, syndactyly, or polydactyly, b) fetal skull bases with pre-dissected IE or the petrous bone, c) fetuses with fragmented IE structures (the cochlea, SSC, PSC, or LSC) during dissection (especially when removing IE en bloc), and d) fetal IEs with signs of any malformations (e.g., hypoplastic cochlea or semicircular canals).

Dissection Stages

Under a surgical microscope (Carl Zeiss Meditec AG, Germany), the senior otologist (D.Ü.T.) of our team performed all dissections through the following steps: a) performing an incision surrounding the skull just above the pinna, b) moving the calvaria laterally, c) removing all soft tissues (e.g., dura, brain, cerebellum, and cranial nerves), d) exposing the petrous part of the temporal bone, e) removing the cartilage tissue on IE, and lastly f) removal of IE as a whole (Figures 1 and 2).

Morphometric Parameters

Fetal IEs were photographed with a millimeter-scaled paper using a digital camera (Nikon d3300 digital camera, Nikon, Tokyo, Japan). All measurements were performed via digital image analysis software (Rasband WS, ImageJ, U.S. National Institutes of Health, Bethesda, Maryland, USA, https://imagej.nih.gov/ij/, 1997-2018). Foot lengths were measured to estimate fetus ages (weeks and months) using a digital caliper (0.01 mm precision, Mahr, 16 ER, Göttingen, Germany). Using this software, all measurements were carried out by the same otorhinolaryngologist (O.G.). The petrous ridge length (PRL),

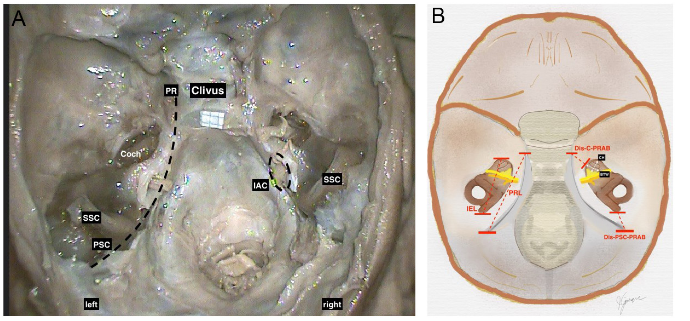

Figure 1. The photographs show the petrous bone (A), and the measured parameters regarding the IE (B). Dis-C-PRAB, the distance of the frontmost part of the cochlea to the most anterior border of the petrous ridge; Dis-SSC-PRPB, the distance of the rearmost part of the superior semicircular canal to the most posterior border of the petrous ridge; IAC, internal acoustic canal; IEL, the length of the IE (the distance of the rearmost part of the posterior semicircular canal to the frontmost part of the cochlea); PR, petrous ridge; PRL, the petrous ridge length (the distance between the most anterior and posterior margins of the petrous ridge); PSC, posterior semicircular canal; SSC, superior semicircular canal.

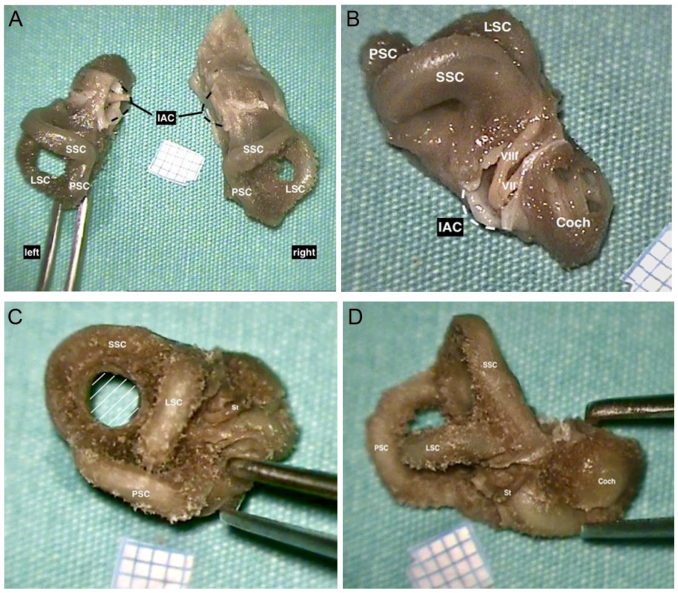

Figure 2. The photograph "A" shows the IE, which was removed en bloc and then cleaned. The photograph "B" shows the IE from a superior aspect. The photograph "C" shows the IE from a posterior aspect. The photograph "D" shows the IE from a lateral aspect. Coch, cochlea; IAC, internal acoustic canal; LSC, lateral semicircular canal; PSC, posterior semicircular canal; SSC, superior semicircular canal; VII, the facial nerve; VIII, the vestibulocochlear nerve.

IE length (IEL), the thickness of bone on the cochlea (BT), the distance of the rearmost part of SSC to the most posterior border of the petrous ridge (Dis-SSC-PRPB), the distance of the frontmost part of the cochlea to the most anterior border of the petrous ridge (Dis-C-PRAB), the width of the basal turn of the cochlea (BTW), the height of the cochlea (CH), the thicknesses of SSC (SSC-T), PSC (PSC-T) and LSC (LSC-T), the inner areas of SSC (SSC-A), PSC (PSC-A) and LSC (LSC-A), the angle between SSC and LSC (Ang-SSC-LSC), the angle between LSC and PSC (Ang-LSC-PSC), and the angle between SSC and PSC (Ang-SSC-PSC) were measured. Moreover, the ratio of IEL to PRL (IEL/PRL) and the ratio of Dis-C-PRAB to Dis-SSC-PRPB (Dis-C-PRAB/Dis-SSC-PRPB) were calculated. The measured parameters related to IE and their definitions are given in Table 1.

Table 1. Definitions, Abbreviations and Units of the Parameters

Parameters	Abbreviations	Unit	Descriptions
Parameters of PR	PRL	mm	The length of PR (the distance between its most anterior and posterior margins)
	IEL	mm	The length of the IE (the distance of the rearmost part of PSC to the frontmost part of the cochlea)
	IEL/PRL		The ratio of IEL to PRL
	BT	mm	The BT
	Dis-SSC-PRPB	mm	The distance of the rearmost part of SSC to the most posterior border of PR
	Dis-C-PRAB	mm	The distance of the frontmost part of the cochlea to the most anterior border of PR
	Dis-C-PRAB/ Dis-SSC-PRPB		The ratio of Dis-C-PRAB to Dis-SSC-PRPB
Parameters of cochlea	BTW	mm	The width of the basal turn of the cochlea
	CH	mm	The CH (the distance between its apex and basal turn)
Parameters of SCs	SSC-T	mm	The thickness of SSC at its middle part
	PSC-T	mm	The thickness of PSC at its middle part
	LSC-T	mm	The thickness of LSC at its middle part
	Ang-SSC-LSC	degree	The angle between SSC and LSC
	Ang-LSC-PSC	degree	The angle between LSC and PSC
	Ang-SSC-PSC	degree	The angle between SSC and PSC
	SSC-A	mm^2	The inner area of SSC
	PSC-A	mm^2	The inner area of PSC
	LSC-A	mm^2	The inner area of LSC

BT, thickness of bone on the cochlea; CH, height of the cochlea; LSC, lateral semicircular canal; PR, petrous ridge; PSC, posterior semicircular canal; SC, semicircular canal; SSC, superior semicircular canal.

Statistical Analysis

The gender comparison was carried out using the independent student's *t*-test, while the side comparison was carried out using the paired student's *t*-test. Changes in the measurements regarding the otic capsule according to gestational weeks (between 19 and 28 weeks) and months (fifth month: 19-20 weeks, sixth month: 21-24 weeks, and seventh month: 25-28 weeks) were analyzed using 1-way ANOVA. Correlations between the measurements regarding the otic capsule were analyzed using the Pearson correlation coefficient test. The normality of the data was checked using the Shapiro–Wilk test. Statistical evaluations were performed using SPSS version 22.0 (IBM SPSS Corp.; Armonk, NY, USA). A "$P < .05$" was considered significant.

RESULTS

No significant difference was observed between the measurements in terms of gender and sides ($P > .05$) (Table 2).

Changes in IE's parameters relative to gestational weeks were presented in Tables 3 and 4. Bone on the cochlea, BTW, CH, Ang-SSC-LSC, Ang-LSC-PSC, and Ang-SSC-PSC did not alter with advancing gestational weeks, but the others increased. Dis-C-PRAB/Dis-SSC-PRPB ($P = .643$) did not change with advancing gestational weeks, whereas IEL/PRL ($P = .037$) decreased.

Alterations in IE's parameters relative to gestational months were presented in Table 5. This table indicated that Dis-C-PRAB/Dis-SSC-PRPB, BTW, CH, Ang-SSC-LSC, Ang-LSC-PSC, and Ang-SSC-PSC did not correlate with gestational months. Bone on the cochlea, SSC-T, PSC-T, LSC-T, SSC-A, PSC-A, and LSC-A did not vary after fifth month. Petrous ridge length, IEL, Dis-SSC-PRPB, and Dis-C-PRAB increased proportionally with advancing gestational months. However, IEL/PRL decreased proportionally with advancing gestational months.

Correlations between the parameters are given in Table 6. We did not observe any correlation between the thicknesses, surface areas, and angulations of the semicircular canals. Basal turn of the cochlea did not correlate with CH. There were positive correlations between

Table 2. Right–Left and Male–Female Comparisons

Parameters	Right	Left	*P*	Male	Female	*P*
PRL	23.63 ± 3.86	24.30 ± 4.72	.734	23.62 ± 3.94	24.32 ± 4.66	.721
IEL	13.18 ± 1.58	13.44 ± 1.39	.694	13.28 ± 1.54	13.34 ± 1.45	.925
IEL/PRL	0.56 ± 0.04	0.56 ± 0.06	.928	0.57 ± 0.05	0.56 ± 0.05	.639
BT	1.24 ± 0.20	1.28 ± 0.21	.690	1.21 ± 0.17	1.32 ± 0.22	.206
Dis-SSC-PRPB	6.83 ± 1.90	6.90 ± 2.15	.938	6.61 ± 1.96	7.11 ± 2.06	.580
Dis-C-PRAB	3.76 ± 0.96	3.94 ± 0.95	.680	3.72 ± 0.82	3.97 ± 1.07	.569
Dis-C-PRAB/Dis-SSC-PRPB	0.56 ± 0.05	0.59 ± 0.11	.388	0.58 ± 0.11	0.56 ± 0.06	.623
BTW	5.70 ± 0.57	6.00 ± 0.50	.232	5.78 ± 0.55	5.93 ± 0.55	.551
CH	4.38 ± 0.69	4.34 ± 0.75	.893	4.14 ± 0.57	4.58 ± 0.77	.163
SSC-T	1.47 ± 0.67	1.30 ± 0.49	.504	1.52 ± 0.70	1.25 ± 0.41	.303
PSC-T	1.29 ± 0.41	1.24 ± 0.45	.784	1.38 ± 0.48	1.15 ± 0.33	.232
LSC-T	1.10 ± 0.37	1.13 ± 0.46	.908	1.24 ± 0.52	0.99 ± 0.21	.172
Ang-SSC-LSC	87.11 ± 5.72	83.99 ± 4.41	.189	84.81 ± 5.80	86.28 ± 4.77	.545
Ang-LSC-PSC	88.63 ± 4.93	87.75 ± 2.69	.624	88.22 ± 4.08	88.16 ± 3.91	.976
Ang-SSC-PSC	89.60 ± 2.61	88.41 ± 2.59	.321	89.52 ± 2.28	88.48 ± 2.92	.387
SSC-A	15.77 ± 4.09	15.36 ± 4.40	.832	14.37 ± 4.14	16.76 ± 3.99	.206
PSC-A	14.79 ± 4.58	12.51 ± 5.05	.303	12.66 ± 3.77	14.64 ± 5.74	.375
LSC-A	11.21 ± 4.91	10.95 ± 5.36	.912	10.01 ± 3.59	12.16 ± 6.12	.350

SSC-T, PSC-T, and LSC-T, and also between SSC-A, PSC-A, and LSC-A. However, the angulations of the semicircular canals did not correlate with each other.

DISCUSSION

Inner ear is the earliest to form among the ear parts. Around the fourth week of the embryonic stage, the otic placode (or the otic disc) on both sides of the myelencephalon occurs as a result of the thickening of the surface ectoderm, which is stimulated by inductive effects from adjacent paraxial mesoderm and notochord. The otic placodes curve inwards from the surface ectoderm and then invaginate down to the mesenchyme immediately beneath them, creating the otic pit. The pit's edges fold toward each other, and their fusion forms the otic vesicle (the bud of the membranous labyrinth). The otic vesicle's connection to the surface ectoderm disappears, and then it gives rise to a diverticulum (which creates the endolymphatic sac and duct). In this stage, the otic vesicle has 2 distinct areas: the dorsal utricular portion (giving rise to the endolymphatic duct, utricle, and semicircular canals) and the ventral saccular portion (giving rise to the cochlear duct and saccule). The inductive effects of the otic vesicle stimulate the surrounding mesenchyme to condense, transforming into the cartilaginous otic capsule. The growth of the membranous labyrinth results in the formation of vacuoles (giving rise to the perilymphatic space) in the otic capsule. The cartilaginous otic capsule ossifies to create the bony labyrinth. Inner ear attains adult shape and dimension in the middle part of prenatal life (around 20-22 weeks).[13]

In this work, PRL, IEL, BT, Dis-SSC-PRPB, and Dis-C-PRAB were measured as 23.97 ± 4.21 mm, 13.31 ± 1.45 mm, 1.26 ± 0.20 mm, 6.86 ±

Table 3. Alterations in the Parameters Related to the Petrous Ridge According to Gestational Weeks

Weeks	PRL	IEL	BT	Dis-SSC-PRPB	Dis-C-PRAB	IEL/PRL	Dis-C-PRAB/Dis-SSC-PRPB
19	17.08 ± 1.16	10.70 ± 0.75	1.08 ± 0.08	3.62 ± 0.47	2.46 ± 0.56	0.63 ± 0.09	0.69 ± 0.24
20	18.31 ± 0.11	11.49 ± 0.35	1.08 ± 0.11	4.63 ± 0.64	2.54 ± 0.25	0.63 ± 0.02	0.56 ± 0.13
21	20.55 ± 0.61	12.05 ± 0.30	1.25 ± 0.33	5.66 ± 0.20	3.04 ± 0.01	0.59 ± 0.00	0.54 ± 0.02
22	23.34 ± 0.08	13.38 ± 0.43	1.15 ± 0.11	6.06 ± 0.10	3.53 ± 0.04	0.57 ± 0.02	0.58 ± 0.02
23	23.62 ± 0.59	13.55 ± 0.17	1.12 ± 0.22	6.52 ± 0.41	3.76 ± 0.23	0.57 ± 0.01	0.58 ± 0.07
24	24.82 ± 0.64	14.11 ± 0.42	1.35 ± 0.18	6.90 ± 0.15	4.36 ± 0.01	0.57 ± 0.00	0.63 ± 0.01
25	26.08 ± 0.97	14.08 ± 1.04	1.25 ± 0.14	7.75 ± 0.14	4.33 ± 0.35	0.54 ± 0.06	0.56 ± 0.03
26	27.79 ± 0.82	13.98 ± 0.46	1.33 ± 0.12	8.31 ± 0.50	4.81 ± 0.11	0.50 ± 0.00	0.58 ± 0.02
27	27.97 ± 1.12	14.70 ± 0.78	1.43 ± 0.01	9.09 ± 0.79	4.55 ± 0.42	0.53 ± 0.01	0.50 ± 0.00
28	30.11 ± 1.15	15.10 ± 0.11	1.60 ± 0.01	10.09 ± 0.46	5.11 ± 0.03	0.50 ± 0.02	0.51 ± 0.02
	23.97 ± 4.21	13.31 ± 1.45	1.26 ± 0.20	6.86 ± 1.97	3.85 ± 0.93	0.56 ± 0.05	0.57 ± 0.09
P	<.001	<.001	.119	<.001	<.001	.037	.643

Table 4. Alterations in the Parameters Related to the Cochlea and Semicircular Canals According to Gestational Weeks

Weeks	BTW	CH	SSC-T	PSC-T	LSC-T	Ang-SSC-LSC	Ang-LSC-PSC	Ang-SSC-PSC	SSC-A	PSC-A	LSC-A
19	5.83 ± 0.82	4.76 ± 0.92	0.87 ± 0.17	1.06 ± 0.29	0.91 ± 0.04	93.39 ± 7.08	92.42 ± 6.53	91.63 ± 0.35	9.84 ± 1.13	8.49 ± 0.12	5.79 ± 0.01
20	5.75 ± 0.18	4.15 ± 0.77	1.01 ± 0.43	1.00 ± 0.40	0.81 ± 0.08	87.70 ± 8.46	83.66 ± 0.40	86.94 ± 3.54	11.35 ± 2.06	6.89 ± 5.10	5.16 ± 1.36
21	5.58 ± 0.09	3.89 ± 0.59	0.98 ± 0.39	0.93 ± 0.31	0.87 ± 0.01	92.20 ± 1.46	91.56 ± 2.33	90.00 ± 5.80	14.35 ± 2.18	10.96 ± 0.66	6.47 ± 0.49
22	6.37 ± 0.14	4.43 ± 0.13	1.29 ± 0.06	1.10 ± 0.07	0.81 ± 0.01	82.69 ± 6.51	85.44 ± 0.55	88.67 ± 0.33	17.05 ± 0.70	15.97 ± 0.64	13.81 ± 1.34
23	6.10 ± 0.28	3.81 ± 0.69	2.65 ± 0.71	2.21 ± 0.23	2.09 ± 0.41	81.48 ± 0.33	83.92 ± 0.78	87.43 ± 4.24	13.39 ± 2.34	11.75 ± 3.01	7.74 ± 0.66
24	6.49 ± 0.70	5.66 ± 0.54	1.03 ± 0.03	1.03 ± 0.10	1.10 ± 0.23	81.35 ± 0.98	86.74 ± 6.84	87.86 ± 1.33	16.78 ± 1.03	15.69 ± 1.41	12.50 ± 1.95
25	5.31 ± 0.12	3.85 ± 0.36	1.26 ± 0.13	1.27 ± 0.06	1.06 ± 0.12	81.02 ± 1.34	90.86 ± 2.18	89.50 ± 2.14	11.35 ± 1.27	10.10 ± 1.62	8.67 ± 1.69
26	5.95 ± 0.27	4.94 ± 0.08	1.37 ± 0.02	1.18 ± 0.16	0.88 ± 0.11	84.73 ± 0.12	90.97 ± 1.13	86.78 ± 0.93	20.20 ± 1.05	18.64 ± 0.04	16.42 ± 0.48
27	5.27 ± 0.21	3.85 ± 0.06	1.54 ± 0.44	1.27 ± 0.34	1.34 ± 0.34	85.51 ± 0.00	88.46 ± 0.08	90.39 ± 1.85	20.24 ± 0.88	17.00 ± 2.55	14.03 ± 0.32
28	5.87 ± 1.10	4.28 ± 0.18	1.87 ± 0.16	1.63 ± 0.26	1.30 ± 0.02	85.44 ± 0.88	87.90 ± 0.66	90.85 ± 0.76	21.11 ± 0.38	21.02 ± 2.35	20.25 ± 0.83
	5.85 ± 0.54	4.36 ± 0.70	1.39 ± 0.58	1.27 ± 0.42	1.11 ± 0.41	85.55 ± 5.22	88.19 ± 3.89	89.00 ± 2.60	15.56 ± 4.14	13.65 ± 4.84	11.08 ± 5.01
P	.374	.072	.008	.012	.001	.108	.146	.639	<.001	.001	<.001

Table 5. Changes in the Parameters According to Gestational Months

Parameters	Fifth Month	Sixth Month	Seventh Month	*P*
PRL	17.70 ± 0.98[a,b]	23.08 ± 1.72[b]	27.99 ± 1.71	<.001
IEL	11.10 ± 0.66[a,b]	13.27 ± 0.85[b]	14.46 ± 0.72	<.001
IEL/PRL	0.63 ± 0.05[a,b]	0.58 ± 0.01[b]	0.52 ± 0.03	<.001
BT	1.08 ± 0.08[a,b]	1.22 ± 0.20	1.40 ± 0.16	.013
Dis-SSC-PRPB	4.12 ± 0.74[a,b]	6.28 ± 0.53[b]	8.81 ± 1.02	<.001
Dis-C-PRAB	2.50 ± 0.36[a,b]	3.67 ± 0.51[b]	4.70 ± 0.38	<.001
Dis-C-PRAB/ Dis-SSC-PRPB	0.63 ± 0.18	0.58 ± 0.05	0.54 ± 0.04	.235
BTW	5.79 ± 0.49	6.13 ± 0.48	5.60 ± 0.55	.138
CH	4.45 ± 0.78	4.45 ± 0.89	4.23 ± 0.50	.805
SSC-T	0.94 ± 0.28[a,b]	1.49 ± 0.79	1.51 ± 0.31	.028
PSC-T	1.03 ± 0.29[a,b]	1.32 ± 0.57	1.34 ± 0.25	.045
LSC-T	0.86 ± 0.08[a,b]	1.22 ± 0.58	1.24 ± 0.25	.036
Ang-SSC-LSC	90.54 ± 7.17	84.43 ± 5.46	84.17 ± 2.07	.096
Ang-LSC-PSC	88.04 ± 6.32	86.91 ± 4.12	89.55 ± 1.76	.422
Ang-SSC-PSC	89.28 ± 3.40	88.49 ± 2.96	89.38 ± 2.05	.789
SSC-A	10.59 ± 1.61[a,b]	15.39 ± 2.12	18.22 ± 4.32	.004
PSC-A	7.69 ± 3.09[a,b]	13.59 ± 2.74	16.69 ± 4.58	.003
LSC-A	5.47 ± 0.87[a,b]	10.13 ± 3.44	14.84 ± 4.55	.002

[a]Comparison to sixth month.
[b]Comparison to seventh month, $P < .05$.

1.97 mm, and 3.85 ± 0.93 mm, respectively. We determined that these parameters, except from BT increased proportionally with advancing gestational weeks and months. Bone on the cochlea did not vary after fifth month. Our mean IEL value seemed to be similar to the average value (11.78 ± 3.92 mm, range: 3.70-17.50 mm) of Jeffery and Spoor,[1] who measured IEL from PSC (its arc's posterior-most point) to the center of the cochlea's basal turn in 41 fetuses aged 9-29 weeks. Dis-C-PRAB/Dis-SSC-PRPB did not change with advancing gestational ages, whereas IEL/PRL decreased despite of proportional increase in PRL and IEL with age. This finding shows that the growth dynamics of IE are slower than that of petrous bone, and thus the area ratio covered by IE in the bone decreased with age. Most of the previous studies report that IE's structures such as the cochlea, semicircular canals, and vestibule reach adult shape and dimension in the early second trimester (i.e., before the 24th week).[1,8,13] We believe that the continued steady increase in IEL in our fetal samples aged from 19 to 28 weeks is due to the development of the vestibule, but not the cochlea or semicircular canals. This interpretation seems to support the study of Honkura et al,[14] who found that the osseous chamber containing the saccule and utricle increased in fetuses aged from 18 to 30 weeks of gestation. Our measurements have clinical implications for prenatal US and MRI examinations. For instance, the cochlea may be identified 1 mm below the plate of the petrous bone (i.e., BT) approximately 4 mm posterior to the petrous apex (i.e., Dis-C-PRAB).

We believe that elucidating the prenatal development of IE anatomic structures will be valuable for the early diagnosis of congenital hearing loss (CHL) and/or balance disorders accompanied by structural disorders, apart from some genetic and toxic etiologies.[4,15] It might be quite effective in prenatal diagnosis, especially considering that

Table 6. Correlations Between the Parameters Related to the Cochlea and Semicircular Canals

	CH	SSC-T	PSC-T	LSC-T	Ang-SSC-LSC	Ang-LSC-PSC	Ang-SSC-PSC	SSC-A	PSC-A	LSC-A
BTW	0.259	−0.017	0.007	0.127	−0.371	−.552*	−0.218	0.115	0.106	0.188
	0.270	0.943	0.978	0.594	0.108	0.012	0.355	0.629	0.655	0.428
CH		−0.392	−0.290	−0.240	−0.043	0.297	−0.015	0.044	0.123	0.193
		0.087	0.215	0.309	0.856	0.203	0.950	0.854	0.604	0.416
SSC-T			.913**	.667**	−0.316	−0.327	−0.029	0.284	0.348	0.256
			<0.001	0.001	0.175	0.160	0.904	0.226	0.132	0.275
PSC-T				.702**	−0.218	−0.185	0.056	0.115	0.205	0.174
				0.001	0.356	0.434	0.813	0.630	0.385	0.464
LSC-T					−0.357	−0.359	−0.005	0.068	0.108	0.064
					0.122	0.120	0.984	0.775	0.652	0.789
Ang-SSC-LSC						0.480	0.350	−0.210	−0.179	−0.315
						0.052	0.130	0.375	0.451	0.176
Ang-LSC-PSC							0.360	−0.091	−0.005	−0.028
							0.119	0.703	0.984	0.908
Ang-SSC-PSC								−0.082	0.042	0.079
								0.731	0.860	0.739
SSC-A									.939**	.897**
									<0.001	<0.001
PSC-A										.920**
										<0.001

*$P < .05$.
**$P < .01$.

the bony labyrinth is affected in approximately 20% of cases with CHL.[16,17] Tilea et al[18] examined in vivo MRI and ex vivo CT images of a 30-week fetus, determining that the fetus had enlarged cochlea and vestibule, occipital meningocele, inferior vermian agenesis, and mild right ventriculomegaly on MRI, and the fetus had cystic dilated vestibules and enlarged cystic cochleas on CT. On account of these reasons, the parents elected to terminate the pregnancy.[18] Moreira et al[19] stated that in vivo MRI provided the opportunity to see IE's components and their possible pathologies, but did not provide sufficient detail in fetuses younger than 25 weeks. On the other hand, Leibovitz et al[4] recommended the use of US in early second trimester fetuses for diagnosing cochlear anomalies as early as possible. We measured BTW and CH as 5.85 ± 0.54 mm and 4.36 ± 0.70 mm, respectively. These parameters did not correlate with gestational ages. Similar to previous studies,[1,4,8] we think that the cochlea attained adult morphology in the early second trimester. We believe that our fetal measurements may be beneficial for clinicians to evaluate in vivo MRI or US views.

In the current work, we measured the thickness, inner surface areas, and angulations of the semicircular canals. Angles between the semicircular canals did not correlate with gestational ages. This finding appears to be consistent with studies in the literature.[1,9] Our Ang-SSC-LSC (85.55 ± 5.22°), Ang-LSC-PSC (88.19 ± 3.89°) and Ang-SSC-PSC (89.00 ± 2.60°) values seemed to resemble the fetal CT study (54 fetuses aged 22-40 weeks) of Mejdoubi et al[9] (Ang-SSC-LSC: 88.67 ± 7.63°, Ang-LSC-PSC: 92.60 ± 6.57° and Ang-SSC-PSC: 90.19 ± 6.99°). They did not observe a correlation between fetal age and these angles and thus stated that the semicircular canals attained a 3-dimensional configuration in the 22nd week.[9] Jeffery and Spoor[1] measured Ang-SSC-PSC as 98.10 ± 6.00° in fetuses and 104.00 ± 5.20° in adults ($P > .05$). Therefore, they determined that the angles between the semicircular canals attained adult 3-dimensional configuration between 17 and 19 weeks.[1] We observed that the thickness and inner surface areas of the semicircular canals correlated with gestational age, but they did not vary after fifth month. In our opinion, the semicircular canals attain adult size between 21 and 24 weeks. This finding seems to be consistent with the literature.[1,10,20] Jeffery and Spoor[1] gave the period for the prenatal labyrinth to reach adult configuration in fetuses as 17-19 weeks. Richard et al[20] reported a later period for SSC (at 24 weeks), PSC (at 25 weeks), and LSC (at 25 weeks) compared to these authors.

Martin et al[21] reported a 3-year-old boy who had a t(2;7)(p14;q21.11) chromosomal translocation. The child was diagnosed with CHARGE syndrome due to the presence of facial anomalies, cranial nerve dysfunction, growth and developmental delays, genital hypoplasia, IE hypoplasia (hypoplastic cochleae and absent semicircular canals), and bilateral choanal atresia.[21] Blaser et al[22] examined IE anomalies in 59 patients with Down syndrome (mean age: 8.13 ± 4.85 years) and observed that the patients commonly had commonly IE dysplasia (hypoplastic cochlea and semicircular canals). Wang et al[23] studied on members of a Chinese family with Branchio-oto-renal syndrome and found IE hypoplasia in some of them. Abu-Amero et al[24] reported a patient with Wildervanck syndrome who had bilateral severe sensorineural hearing loss due to bilateral IE malformations (e.g., dilated cochlea, absent or dilated semicircular canals, and absent or dilated vestibule). In some congenital malformations, patients have dilated or hypoplastic IEs; however, these anomalies, such as hypoplastic or dilated cochlea and/or semicircular canals, are generally detected in early or late pediatric ages.[21-24] If analyses regarding IE abnormalities are performed during routine pregnancy screenings, IE pathologies may be determined while still in the womb. Algorithms used in routine pregnancy scans include morphometric parameters such as nuchal translucency, biparietal diameter, and head circumference, but they do not include any measurement related to IE. In this regard, we think that our IEL/PRL ratio may be beneficial for clinicians to detect IE malformations for the following reasons: a) as it would be time-consuming to observe IE's structures (the cochlea, vestibule, SSC, PSC, or LSC) separately and needs thorough experience and knowledge to assess their pathologies with US, this ratio may be useful to form a preliminary opinion as to whether an IE anomaly is present or not; b) midterm fetuses with suspected IE anomalies may be referred for further investigations such as fetal MRI; c) parents learn about the child's possible pathologies like hearing impairment at an early time; and d) after birth, babies with IE anomalies may be referred to ENT clinics as early as possible to ensure early interventions. This study presented IEL/PRL ratios from the 19th week (0.63 ± 0.09) to the 28th week (0.50 ± 0.02). In our opinion, values outside the standard interval in the IEL/PRL ratio may be a clue for detecting IE anomalies such as dilated or hypoplastic cochlea and/or semicircular canals. Considering the association of IE anomalies with many genetic malformations, we believe that it would be very useful to include IE-related measurements in routine pregnancy screening.

Today, although important steps have been taken in prenatal screening, there are still some points where data and practice are insufficient. Prenatal developmental stages of IE are one of the issues where there is a lack of knowledge. In routine obstetric practice, screening of the fetus for some structural and genetic disorders has taken place. In cases of fetal anomalies that cause serious morbidity or mortality as a result of screening and diagnostic examinations, processes leading to pregnancy termination are involved.[25] On the other hand, identification of certain structural disorders that do not require termination provides guidance for both the family and physicians in terms of postnatal follow-up and treatment. The mid-trimester obstetric ultrasound, a cornerstone of modern prenatal care, is an imaging technique that all women are offered as a routine examination between about 18 and 24 weeks of gestation. This US screening offers information on the detection of structural abnormalities and fetal development.[26] Fetal head, neck, face, chest, heart, abdomen, and skeletal system are the suggested minimum requirements for a basic fetal anatomical survey. The examination of the skull includes assessment of its size, shape, integrity, and bone density. The basic examination of the brain includes transventricular and transthalamic planes for the assessment of the hemispheres, and the transcerebellar plane for the assessment of the posterior fossa.[26] When a central nervous system (CNS) malformation is suspected on this US scan, confirmation is usually made with fetal MRI, regarding its superiority on soft tissue contrast and ability to demonstrate sulcation and myelination. Therefore, ultrasound abnormalities are often confirmed or ruled out by MRI, particularly for CNS malformations. IE structures are not included in the obstetric routine US screening, although IE anomalies are recognized as a subset of fetal anomalies.[27] Superior semicircular canal hypoplasia, posterior labyrinthine anomalies, and cochlear anomalies are some examples that have been shown to be associated with genetic disorders such as Walker–Warburg syndrome, CHARGE syndrome, and Trisomy 13.[27] Sensorineural hearing loss and balance dysfunction in neonates are also morbidities that can be predicted with prenatal US screening of IE. Therefore, development and possible abnormalities of IE and their role among other system malformations also deserve to be focused more detail. The authors would like to point out that focusing on skull base and IE evaluation in prenatal screening will contribute to directing diagnosis and treatment modalities.

Our investigation possesses some limitations. First, this work included a limited number of fetal cadavers aged 19-28 years. This was due to a) the presence of a limited number of fetuses in our inventory, b) the exclusion of fetuses used in previous otologic studies, and c) the exclusion of fetuses damaged during en bloc removal of IE. The main concern we aimed to address was to use the fetuses without any tissue damage of the tissues (the cochlea, SSC, PSC, or LSC) that occurred during en bloc IE removal. To obtain accurate data and statistics, entire fetus was excluded from the study, even in cases of small unilateral tears in IE's structures. This situation led to a significant reduction in the sample size of the study. Second, the study did not contain CT or MRI images of fetuses. Third, fetal cadavers were fixed with 10% formalin, leading to hardening and color changes in tissues. Therefore, further radio-anatomic studies with a larger number of fresh or fresh-frozen fetal cadavers are needed. In addition, further study populations with a more homogeneous distribution in terms of age (i.e., all midterm fetuses aged between 13 and 28 weeks of gestation) and gender would contribute to a clearer understanding of the development of IE within the petrous bone. Nevertheless, we think that this study may be important for otologists and neurotologists to see the relation of IE with the petrous bone.

CONCLUSION

The relation of IE abnormalities and related perinatal morbidities should be taken into consideration and deserves to be focused more in detail. Our findings may be useful for otologists to see the relation of IE with the petrous bone. Our numeric dataset may form a basis of prenatal US and MRI investigations for obstetricians and neuroradiologists.

Availability of Data and Materials : The data that support the findings of this study are available on request from the corresponding author.

Ethics Committe Approval: This study was approved by the Ethics Committee of Mersin University (approval no.: 2022/463, date: July 6, 2022).

Informed Consent: Approval from the Ethics Committee of Mersin University was obtained and in keeping with the policies for a retrospective review, informed consent was not required.

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