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Intrauterine Growth References for Turkish Infants

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What is already known on this topic?

- *Fetal growth is known to be affected by ethnic and environmental factors; therefore, intrauterine growth references for each community vary and need to be determined individually.*

What this study adds on this topic?

- *Using these new references, the intrauterine growth of Turkish infants and postnatal growth of those born prematurely can be followed up more effectively.*
- *It will be possible to more accurately determine if Turkish infants are small for gestational age or large for gestational age.*

ABSTRACT

Objective: Fetal growth is known to be affected by ethnic and environmental factors; therefore, intrauterine growth references for each community vary and need to be determined individually. This study aimed to construct intrauterine growth references for Turkish infants.

Materials and Methods: This prospective, multicenter, cross-sectional study was performed in collaboration with the Turkish Ministry of Health and the Turkish Neonatology Society, in coordination with Mersin University. The study included 33 healthcare centers from all regions of Türkiye. The study included singleton infants who were born alive at 24-42 weeks of gestation. Weight, length, and head circumference were measured within the first 4 hours of delivery. The Lambda–Mu–Sigma method and penalized likelihood were used to establish the curves and construct percentiles.

Results: In all, data from 10 286 infants were analyzed and 552 cases that did not meet the inclusion criteria were excluded. The intrauterine growth curves and tables for Turkish infants were constructed using the data for 9734 singleton infants born at 24-42 weeks of gestation.

Conclusion: To the best of our knowledge this is the first study to establish intrauterine growth references for Turkish infants, based on a cohort of infants from all regions of Türkiye. Using these new references, the intrauterine growth of Turkish infants and postnatal growth of those born prematurely can be followed-up more effectively, and it will be possible to more accurately determine if Turkish infants are small for gestational age or large for gestational age.

Keywords: Infants, intrauterine growth references, large for gestational age, small for gestational age, Turkish

INTRODUCTION

One of the important measurements during physical examination of newborns is determination of whether the infant's weight, length, and head circumference are appropriate for their gestational age.[1,2] When the anthropometric measurements of a newborn are not appropriate for their gestational age, it may indicate the presence of a variety of disorders or diseases. In addition, infants born small for gestational age (SGA) or large for gestational age (LGA) can develop multiple problems early or late in life. For example, SGA infants can develop such conditions as hypothermia and hypoglycemia in the early postnatal period, and premature adrenarche, obesity, short stature, polycystic ovary syndrome, hypertension, dyslipidemia, cardiovascular diseases, insulin resistance, and type 2 diabetes mellitus later in life.[3-8] On the other hand, LGA infants have an increased risk of birth trauma, hypoglycemia, and hypocalcemia during the early postnatal period, and metabolic syndrome during adulthood.[9,10] Intrauterine growth references play a major role in the follow-up of growth in premature infants.[11]

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Intrauterine growth references were first published by Lubchenco et al[12] in 1966. Their references, originally obtained from the data for infants born at Colorado General Hospital, are still widely used worldwide; however, more recently many countries have begun to establish intrauterine growth references specific to their own country.[13-19] The present study aimed to establish for the first time intrauterine growth references for Turkish infants, based on a large nation-sample.

MATERIALS AND METHODS

This prospective, multicenter, cross-sectional study was performed between January 2006 and December 2010 in collaboration with the Turkish Ministry of Health and the Turkish Neonatology Society, in coordination with Mersin University. The study protocol was approved by the Mersin University Clinical Research Ethics Committee on November 9, 2022 with the approval number of 749. Verbal and written informed consent was obtained from the patients' parents who agreed to take part in the study. The study included 33 healthcare centers from all regions of Türkiye. Seven of these centers were located in the Marmara Region, 7 in the Aegean Region, 7 in the Central Anatolia Region, 4 in the Mediterranean Region, 4 in the Black Sea Region, 3 in Eastern Anatolia Region, and 1 in the Southeastern Anatolia Region. Weight, length, and head circumference of infants born at the participating centers were measured within the first 4 hours of birth. Weight measurements were performed while infants were naked using electronic scales with 1-5-g accuracy. Length was measured using standard wooden rulers. Head circumference was measured through the largest occipitofrontal points, using standard measurement strips. Gestational age was calculated on the basis of ultrasonography measurements performed during the first trimester of pregnancy or based on the date of the last menstrual period.

Inclusion and Exclusion Criteria

Live-born singleton Turkish citizen infants born at 24-42 weeks of gestation were included in the study. Exclusion criteria included uncertain gestational age, non-singleton birth, congenital anomalies, intrauterine infection, diagnosis of hydrops fetalis, stillbirth, and the presence of any significant maternal disease that can affect fetal growth, such as diabetes mellitus, systemic lupus erythematosus, severe hypertension, and severe anemia.

Sample Size Determination

A preliminary study was conducted to determine the number of infants born at each gestational week that should be included in the study. This preliminary study included 532 infants born alive at 24-42 weeks of gestation at Mersin University Hospital who met the inclusion criteria. It was calculated that ≥100 infants born at each gestation week must be included in the study to obtain 95% reliability. Based on the results of this preliminary study, it was planned to include 100 infants born at each gestational week (weeks 24-42) in the study.

Statistical Analysis and Establishment of Curves

Statistical analysis was performed using the Statistical Packaage for the Social Sciences for Windows version 11.5 (SPSS, Inc., Chicago, Ill, USA). Kolmogorov–Smirnov normality test was used to decide the normality of distribution. Outliers were identified using a box-plot diagram and were then excluded from the study. Mean ± SD values were derived from descriptive statistics for constant variables of weight, length, and head circumference. Student's *t*-test (independent *t*-test), a parametric test for comparing the means of 2 independent groups, was used to compare the means of weight, length, and head circumference between sexes. The level of statistical significance was set at $P < .05$. The Lambda–Mu–Sigma (LMS) method and penalized likelihood (LMS Growth Program, Medical Research Council, Cambridge, UK) were used to establish the curves and construct percentiles. Values corresponding to the third, fifth, 10th, 25th, 50th, 75th, 90th, 95th, and 97th percentiles were determined via LMS and penalized likelihood, and then percentile curves were constructed.

RESULTS

In total, data for 10286 infants born at 33 healthcare centers were assessed. In all, 9734 infants were included in the study and 552 who did not meet the study inclusion criteria were excluded. Among the infants, 52.2% were male and 47.8% were female. Mean ± SD maternal age was 28.5 ± 5.6 years (range: 16-48 years). There weren't any significant differences in weight, length, or head circumference between the male and female infants born at gestational weeks 24-36 ($P > .05$). In contrast, weight, length, and head circumference of the infants born at gestational weeks 37-42 did differ significantly according to sex (Table 1). As such, sex-specific reference values for males and females born at 37-42 weeks of gestation are given in the percentile tables (Tables 2-4). Intrauterine growth curves are presented separately for all gestational weeks according to sex for ease of use (Figures 1-6).

DISCUSSION

The intrauterine growth references published by Lubchenco et al[12] and Fenton and Kim[20] are commonly used to diagnose SGA and LGA in Turkish infants.[21,22] As fetal growth is affected by ethnic characteristics and environmental factors,[23,24] these previously published references, which are specific to their communities, may not be appropriate for assessing intrauterine growth in Turkish infants. A few studies have examined intrauterine growth references in Turkish infants; however, they were conducted using data from hospitals in a single Turkish city.[25-27] As such, the references the studies produced have not found widespread use in Türkiye. The present study, in contrast, included a large sample from all regions of Türkiye and, therefore, we think the obtained intrauterine growth references will be widely used in Türkiye, increasing the accuracy of the diagnosis of SGA and LGA in Turkish infants. To the best of our knowledge, this is the first study to establish intrauterine growth references for Turkish infants, based on a cohort of infants from all regions of Türkiye.

Thanks to treatment advances, survival of premature infants has increased significantly worldwide. The primary goal of neonatologists today is to achieve the best neurodevelopmental outcomes in preterm infants. One of the most important factors associated with good neurodevelopmental outcomes in preterm infants is ensuring that they grow sufficiently during the postnatal period.[28-30] As such, the growth of premature infants should be closely monitored in both neonatal intensive

Table 1. Mean and Standard Deviation Values of Birth Weight, Height, and Head Circumference Measurements of Male and Female Babies Between 37 and 42 weeks of Gestation According to Their Gestational Ages, and *P*-values of the Differences Between the Measurements

		Birth Weight (g)			Birth Length (cm)			Head Circumference (cm)		
GA (w)	Gender	Mean	SD	*P*	Mean	SD	*P*	Mean	SD	*P*
37	Male	3171.71	483.67	.021	48.28	2.51	.009	34.44	1.30	.001
	Female	3069.92	436.34		48.06	2.16		34.24	1.33	
38	Male	3318.22	422.22	<.001	49.20	1.99	<.001	34.95	1.47	<.001
	Female	3245.60	441.17		48.98	1.91		34.50	1.25	
39	Male	3445.44	430.65	<.001	49.68	1.87	<.001	35.15	1.31	<.001
	Female	3285.49	385.64		49.10	2.16		34.46	1.31	
40	Male	3520.85	440.26	<.001	50.03	2.18	<.001	35.05	1.33	<.001
	Female	3329.12	426.63		49.58	1.76		34.60	1.29	
41	Male	3660.80	534.82	<.001	50.63	2.02	< .001	35.82	2.07	<.001
	Female	3456.04	508.72		50.11	1.93		34.81	1.24	
42	Male	3653.16	383.52	.018	50.87	1.53	.043	35.59	1.00	.040
	Female	3423.33	341.72		49.58	1.00		35.04	1.18	

GA, gestational age; w, week.

care units and neonatal outpatient clinics. Ideally, it is aimed for preterm infants to grow as during the intrauterine period;[31] therefore, we think the intrauterine growth references presented in this study will be useful for effectively monitoring the growth of premature Turkish infants.

It is known that sex affects intrauterine growth and that intrauterine growth in males and females differ.[32] In the present study, there were significant differences between the sexes in birth weight, head circumference, and length for each week starting from the 37th gestational week; therefore, reference values are given separately in the percentile tables according to sex for gestational weeks 37-42.

The most important limitation of the present study is that the sample size of infants born at gestational weeks 24-25 was smaller than intended. This limitation should be kept in mind when evaluating infants born at 24-25 weeks of gestation.

Table 2. Birth Weight for Turkish Infants According to Gestational Age

			Birth Weight Percentages (g)								
GA (w)	No of Cases	Sex	Third	Fifth	10th	25th	50th	75th	90th	95th	97th
24	48	All	429	492	589	645	700	797	840	850	977
25	59	All	510	540	600	670	760	930	1000	1040	1230
26	101	All	574	650	680	785	920	1050	1200	1327	1384
27	117	All	653	700	747	860	990	1095	1266	1344	1398
28	196	All	693	805	903	1050	1217	1400	1558	1690	1716
29	127	All	777	822	931	1150	1270	1450	1600	1707	1800
30	221	All	890	940	1100	1280	1490	1665	1882	2095	2240
31	252	All	991	1030	1203	1400	1605	1807	2000	2200	2366
32	426	All	1288	1360	1457	1650	1840	2060	2260	2395	2500
33	389	All	1328	1380	1510	1790	2000	2200	2420	2590	2679
34	489	All	1330	1420	1650	1900	2190	2450	2700	2957	3169
35	247	All	1588	1750	1888	2050	2400	2830	3354	3419	3600
36	536	All	1800	1900	2064	2320	2680	3000	3300	3500	3638
37	725	Male	2151	2209	2440	2720	3055	3387	3600	3850	3959
		Female	2150	2200	2438	2650	2970	3250	3502	3792	3905
38	1899	Male	2413	2537	2705	3000	3300	3550	3850	3997	4108
		Female	2300	2470	2616	2883	3150	3429	3688	3872	3934
39	1976	Male	2640	2740	2890	3120	3400	3700	3959	4110	4200
		Female	2522	2608	2790	3000	3230	3500	3794	3966	4124
40	1230	Male	2745	2860	3000	3220	3500	3800	4072	4220	4308
		Female	2560	2680	2836	3080	3350	3640	3884	4071	4204
41	461	Male	2752	2910	3040	3300	3586	3850	4133	4280	4310
		Female	2569	2690	2850	3166	3435	3670	3950	4200	4265
42	122	Male	2865	2982	3048	3360	3600	3995	4342	4535	5150
		Female	2633	2764	2900	3150	3470	3745	4014	4385	4524

GA, gestational age; w, week.

Table 3. Length of Turkish Infants According to Gestational Age

Birth Length Percentiles (cm)											
GA (w)	**No of Cases**	**Sex**	**Third**	**Fifth**	**10th**	**25th**	**50th**	**75th**	**90th**	**95th**	**97th**
24	47	All	25.4	26.4	27.8	29.0	31.0	33.0	35.0	36.6	37.0
25	57	All	25.7	26.9	28.9	30.0	33.0	35.0	37.0	38.1	39.0
26	98	All	28.9	29.9	30.3	32.7	34.5	37.0	38.0	39.0	39.5
27	112	All	29.0	30.0	31.0	33.0	35.0	37.1	40.0	41.0	42.0
28	185	All	31.0	32.0	33.0	36.0	38.0	40.0	43.0	44.0	45.0
29	122	All	31.1	32.6	34.0	36.1	39.0	40.1	43.1	44.1	45.2
30	218	All	32.0	33.0	36.0	38.0	40.0	43.0	45.0	46.0	46.4
31	247	All	35.0	36.0	37.4	40.0	41.0	44.0	46.0	47.0	47.5
32	417	All	37.0	37.9	39.9	41.0	43.0	45.0	47.0	47.5	48.0
33	384	All	37.5	38.0	40.0	42.0	44.0	46.0	48.0	48.1	49.0
34	480	All	38.4	40.0	41.0	43.5	45.0	47.0	48.9	49.0	50.0
35	233	All	40.0	41.0	43.0	45.0	46.0	48.0	50.0	51.0	51.1
36	525	All	41.0	42.0	43.3	45.1	47.0	49.0	50.1	51.1	51.3
37	709	Male	43.0	44.0	45.0	47.0	48.0	50.0	51.0	51.5	52.0
		Female	42.8	43.7	44.7	46.0	47.9	49.2	50.6	51.2	51.8
38	1838	Male	45.0	46.0	47.0	48.0	49.0	50.5	51.7	52.0	53.0
		Female	44.0	45.0	46.0	47.6	48.7	50.0	51.0	51.3	52.0
39	1899	Male	46.0	46.5	48.0	49.0	50.0	51.0	52.0	53.0	53.2
		Female	45.8	46.0	47.0	48.0	49.0	50.4	51.4	52.0	52.1
40	1136	Male	46.5	47.0	48.3	49.4	50.6	51.5	52.1	53.4	53.7
		Female	46.1	46.8	47.5	48.8	50.0	51.0	52.0	53.0	53.2
41	440	Male	47.0	47.2	48.5	49.6	50.8	51.7	53.0	54.0	55.0
		Female	46.4	47.0	47.8	49.0	50.2	51.2	52.4	53.1	53.5
42	120	Male	47.8	48.0	49.0	50.0	51.0	52.0	53.6	55.5	56.0
		Female	46.8	47.2	48.0	49.3	50.4	51.4	52.5	54.0	54.9

GA, gestational age; w, week.

Table 4. Head Circumference of Turkish Infants According to Gestational Age

Head circumference percentiles (cm)											
GA (w)	**No of cases**	**Sex**	**Third**	**Fifth**	**10th**	**25th**	**50th**	**75th**	**90th**	**95th**	**97th**
24	47	All	19.4	20.0	20.2	21.5	22.5	24.0	26.0	26.6	27.5
25	55	All	19.6	20.5	21.3	22.0	23.0	25.0	27.0	28.1	28.6
26	97	All	21.0	22.0	22.7	23.0	25.0	26.0	28.0	29.1	30.0
27	114	All	22.5	23.0	23.2	24.0	25.5	27.0	28.2	29.2	30.5
28	189	All	22.8	24.0	24.3	26.0	27.0	28.8	30.0	31.7	32.0
29	124	All	23.3	24.2	25.0	26.2	27.5	29.0	30.5	32.0	33.2
30	215	All	24.7	25.4	26.0	27.0	29.0	30.0	31.0	32.1	33.0
31	249	All	26.0	26.3	27.0	28.0	29.4	30.8	32.0	33.0	34.0
32	408	All	27.0	27.5	28.0	29.0	30.5	32.0	33.0	34.0	34.4
33	377	All	27.2	27.6	28.2	30.0	31.0	32.3	33.4	34.2	34.5
34	471	All	28.0	28.9	30.0	30.5	32.0	33.0	34.0	35.0	35.1
35	229	All	29.0	29.2	30.2	31.0	32.5	34.0	35.0	35.1	36.0
36	518	All	30.0	30.2	31.0	32.0	33.0	34.2	35.3	36.0	36.3
37	699	Male	31.4	32.0	32.3	33.2	34.2	35.0	36.0	37.0	37.1
		Female	31.0	31.9	32.0	33.0	34.0	34.6	35.8	36.2	36.5
38	1816	Male	32.0	32.5	33.0	33.9	35.0	35.5	36.5	37.1	37.2
		Female	31.8	32.0	32.7	33.8	34.5	35.0	36.0	36.5	36.8
39	1861	Male	32.5	33.0	33.5	34.0	35.1	36.0	36.8	37.2	37.5
		Female	32.0	32.5	33.0	33.9	34.9	35.4	36.1	36.7	37.0
40	1132	Male	33.0	33.2	33.6	34.1	35.2	36.2	37.0	37.3	37.6
		Female	32.2	32.7	33.1	34.0	35.0	35.5	36.2	36.9	37.1
41	431	Male	33.1	33.3	34.0	34.5	35.5	36.3	37.2	37.7	38.0
		Female	32.5	33.0	33.2	34.1	35.1	35.6	36.3	37.0	37.3
42	119	Male	33.3	33.5	34.2	34.8	35.7	36.5	37.4	37.8	38.1
		Female	32.6	33.1	33.4	34.2	35.2	36.0	36.5	37.4	37.6

GA, gestational age; w, week.

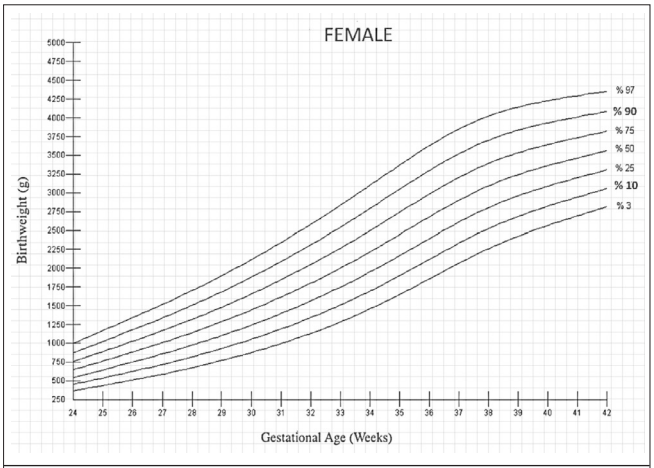


Figure 1. Birth weight curves for female according to gestational age.

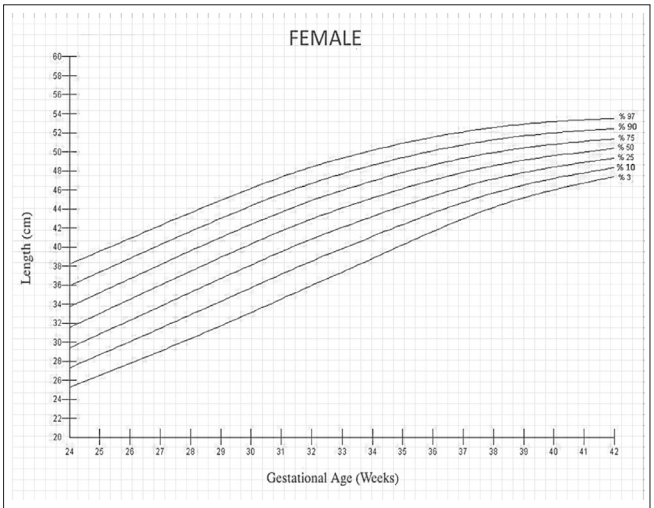


Figure 2. Length curves for female according to gestational age.

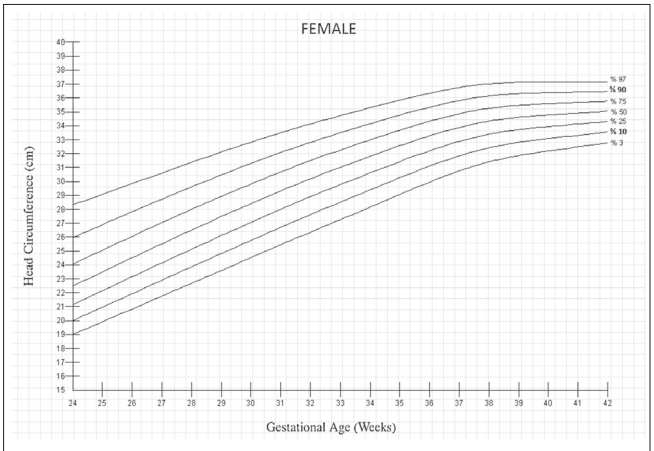


Figure 3. Head circumference curves for female according to gestational age.

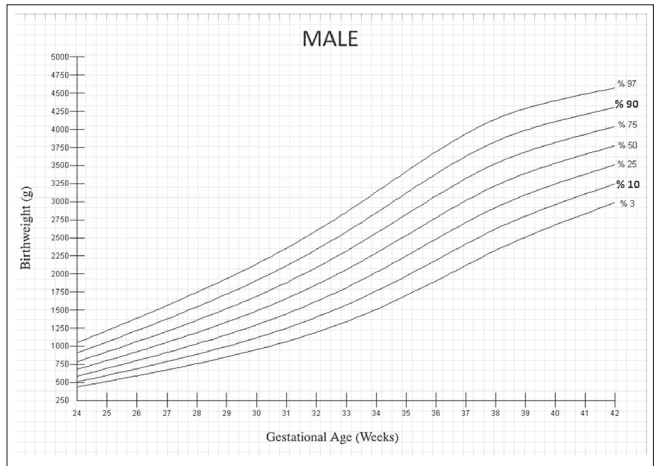


Figure 4. Birth weight curves for male according to gestational age.



Figure 5. Length curves for male according to gestational age.

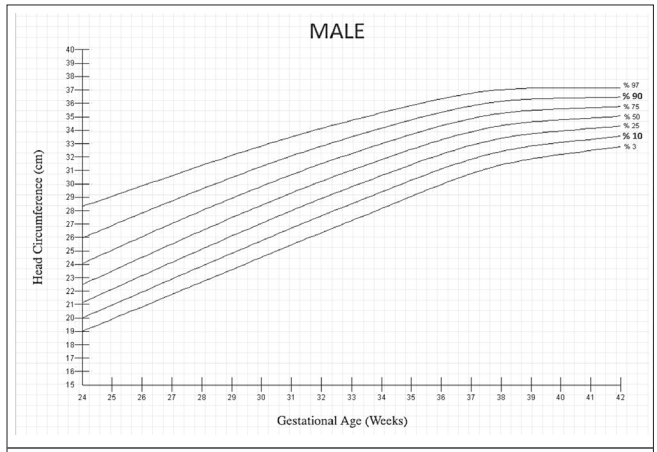


Figure 6. Head circumference curves for male according to gestational age.

In contrast, the number of cases included in the study born at other gestational ages is sufficient and, therefore, those references can be confidently used for Turkish infants born at gestational weeks 26-42. We think that the sample sizes in the groups with insufficient cases may be increased to form intrauterine growth references for these groups in the future.

In conclusion, the present prospective, multicenter, cross-sectional study established intrauterine growth references based on measurements of weight, length, and head circumference for Turkish infants born at 24-42 weeks of gestation.

These references will facilitate an increase in the accuracy of the diagnosis of SGA and LGA in Turkish infants, and provide more accurate growth references for preterm Turkish infants during the postnatal period than have been previously available.

List of Centers Where the Study Was Conducted: Ankara Etlik Zübeyde Hanım Women's Health, Training and Research Hospital, İzmir Ege Women's Health, Training and Research Hospital, Çukurova University Hospital, Gazi University Hospital, Dokuz Eylül University Hospital, Ankara University Hospital, Akdeniz University Hospital, Pamukkale University Hospital, Erciyes University Hospital, Erzurum Nenehatun Obstetrics and Gynecology Hospital, Kocaeli University Hospital, Hacettepe University Hospital, Trakya University Hospital, Mersin University Hospital, Ege University Hospital, Marmara University Hospital, Ondokuz Mayıs University Hospital, Adnan Menderes University Hospital, Van Obstetrics and Pediatrics Hospital, Diyarbakır Obstetrics and Pediatrics Hospital, Bursa Zübeyde Hanım Obstetrics and Gynecology Hospital, Trabzon Obstetrics and Pediatrics Hospital, Uludağ University Hospital, Kayseri Obstetrics and Pediatrics Hospital, Dr. E. Hayri Üstündağ Gynecology and Obstetrics Hospital, VKV American Hospital, Balıkesir Obstetrics and Pediatrics Hospital, Celal Bayar University Hospital, Samsun Obstetrics and Pediatrics Hospital, Atatürk University Hospital, Süleyman Demirel University Hospital, Karadeniz Technical University Hospital, Dr. Sami Ulus Gynecology Obstetrics and Child Health, and Diseases Training and Research Hospital.

Ethics Committee Approval: This study was approved by the Ethics Committee of Mersin University (approval no: 749; date: November 9, 2022).

Informed Consent: Verbal and written informed consent was obtained from the patients' parents who agreed to take part in the study.

Peer-review: Externally peer-reviewed.

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Declaration of Interests: The authors have no conflict of interest to declare.

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