

11. Li M, Xu B, Yu H, Wan Y, Zhu Z, Luo P, et al. Associations between serum lipid profiles and the incidence of chronic obstructive pulmonary disease in the UK Biobank. *Journal of Health, Population and Nutrition*, 2025; 44(1), 281. <https://doi.org/10.1186/s41043-025-01026-716>.
12. Liang Q, Wang Y, Li Z. Lipid metabolism reprogramming in chronic obstructive pulmonary disease. *Mol Med*. 2025 31, 129. <https://doi.org/10.1186/s10020-025-01191-9>.
13. Ozlu T, Sengoren DO, Turkis FC, Degirmenci C, Ilgazlı A, Gülmez I, et al. Clinical and Functional Heterogeneity of COPD Phenotypes: A Multicenter Study from Turkey (DIPTUR Study). *Medicina*. 2026; 62(2):402. <https://doi.org/10.3390/medicina62020402>.
14. Tudoric N, Koblicez V, Miravittles M, Valipour A, Milenkovic B, Barczyk A, et al. GOLD 2017 on the way to a phenotypic approach? Analysis from the Phenotypes of COPD in Central and Eastern Europe (POPE) Cohort. *Eur Respir J*. 2017 Apr 26;49(4):1602518. doi: 10.1183/13993003.02518-2016.
15. Vicol C, Buculei I, Melinte OE, Dobrin ME, Stavarache EI, Gavrilescu CM, et al. The Lipid Profile and Biochemical Parameters of COPD Patients in Relation to Smoking Status. *Biomedicine*. 2022 Nov 15;10(11):2936. doi: 10.3390/biomedicine10112936.
16. Zeng Y, Wang X, Lin X. Associations between serum lipid profiles and the incidence of chronic obstructive pulmonary disease in heavily smoking cohorts. *Respiratory Research*. 2025; 26(1):102–114.
17. Zhao S, Zheng L, Zhu M, Shui Y, Bao X, Zhao J. Intensive Intervention Improves Outcomes for Chronic Obstructive Pulmonary Disease Patients: A Medical Consortium-Based Management. *Can Respir J*. 2022 Jun 27;2022:6748330. doi: 10.1155/2022/6748330.

Conflict of interest. The authors have no conflicts of interest to declare.

ORCID: Musayeva A.K. <https://orcid.org/0009-0005-7378-0102>, Farajova N.A. <https://orcid.org/0000-0002-9227-5743>, Ismayilova N.R. <https://orcid.org/0009-0005-0006-2580-0321>, Huseynova N.N. <https://orcid.org/0009-0005-7388-3419>, Mehdiyev S.K. <https://orcid.org/0000-0001-5970-0456>.

Article received: 9.07.2025

DOI 10.26724/2079-8334-2026-3-97-119-123

UDC 618.17-053.6

Mustafayeva I.R., Aliyeva E.M., Garashova M.A.
Azerbaijan Medical University, Baku, Azerbaijan

CHARACTERISTICS OF PUBERTAL DEVELOPMENT IN ADOLESCENT GIRLS BORN WITH LOW BIRTH WEIGHT

e-mail: mic_amu@mail.ru

Low birth weight is considered a significant risk factor for impaired physical, pubertal, and reproductive development in girls. This study aimed to investigate reproductive organ development during puberty in girls born with low birth weight. The study included 65 adolescent girls aged 14–17 years who were born at term with a birth weight of 1,900–2,500 g; the control group comprised 30 healthy age-matched girls. Anthropometric parameters, secondary sexual characteristics, and ultrasonographic measurements of the uterus and ovaries were assessed. Girls born with low birth weight had significantly lower height, body weight, and pelvic dimensions than controls ($p < 0.05$). Delayed breast development, more pronounced axillary and pubic hair growth, and moderate hirsutism were observed. Ultrasonography revealed significantly smaller uterine dimensions, reduced endometrial thickness, and lower bilateral ovarian volumes ($p < 0.05$). These findings indicate delayed physical and pubertal development and may suggest impaired reproductive system maturation in girls born with low birth weight.

Key words: low birth weight, puberty, adolescent girls, reproductive development, ultrasonography.

Мустафасва І.Р., Алієва Е.М., Гарашова М.А.

ОСОБЛИВОСТІ ПЕРЕБІГУ ПЕРІОДУ СТАТЕВОГО ДОЗРІВАННЯ У ДІВЧАТОК З НИЗЬКОЮ МАСОЮ ТІЛА ПРИ НАРОДЖЕННІ

Низька маса тіла при народженні вважається значущим фактором ризику порушень фізичного, статевого та репродуктивного розвитку дівчаток. Метою дослідження було вивчення особливостей розвитку репродуктивних органів у період статевого дозрівання у дівчаток, які народилися з низькою масою тіла. Було обстежено 65 дівчат-підлітків віком 14–17 років, які народилися доношеними з масою тіла 1900–2500 г; контрольну групу склали 30 здорових однолітків. Оцінювали антропометричні показники, вторинні статеві ознаки та ультразвукові параметри матки й яєчників. У дівчаток із низькою масою тіла при народженні виявлено статистично значуще менші показники зросту, маси тіла та розмірів таза порівняно з контрольною групою ($p < 0.05$). Відзначалися затримка розвитку молочних залоз, більш виражене оволосіння в пахвових та лобкових ділянках та помірний гірсутизм. Під час ультразвукового дослідження було встановлено менші розміри матки, товщину ендометрія та об'єм обох яєчників ($p < 0.05$). Отримані результати свідчать про затримку фізичного та статевого розвитку та можливе порушення дозрівання репродуктивної системи у дівчаток, які народилися з низькою масою тіла.

Ключові слова: низька маса тіла при народженні, дівчата-підлітки, пубертатний період, репродуктивне здоров'я, гірсутизм, ультразвукове дослідження.

Preservation of reproductive health in adulthood largely depends on normal growth and maturation during childhood and adolescence. Fetal and early postnatal growth are increasingly recognized as important determinants of pubertal

timing and later endocrine and reproductive health [1–5].

Adverse intrauterine conditions may affect fetal growth and initiate long-term developmental adaptations. Current evidence links fetal growth

restriction, low birth weight, and small-for-gestational-age birth with persistent changes in somatic growth, metabolic regulation, endocrine function, and reproductive development extending from childhood into adulthood [4, 11, 16].

Children born with fetal growth restriction or low birth weight may demonstrate incomplete catch-up growth and altered body composition during childhood and adolescence [6, 7, 9]. The developmental-programming concept further suggests that intrauterine growth disturbances may produce metabolic and epigenetic adaptations that persist after birth [11–13].

Fetal and infant growth are also associated with the timing and pattern of pubertal development. Prospective studies have demonstrated relationships between birth size, postnatal growth trajectories, and pubertal onset, indicating that both prenatal growth and subsequent catch-up growth may influence maturation in girls [1–3, 5].

The potential reproductive consequences of impaired early growth extend beyond pubertal timing. Endocrine and metabolic abnormalities have been described in adolescents and adults born small for gestational age, while studies of women born preterm or with low birth weight have evaluated hyperandrogenic features, menstrual characteristics, hormonal profiles, and later reproductive outcomes [8, 10, 14, 15]. These observations support long-term assessment of reproductive health in girls with a history of low birth weight.

The purpose of the study was to evaluate the characteristics of reproductive organ development during puberty in girls with a history of low birth weight.

Materials and methods. A cross-sectional study was conducted among 65 adolescent girls born with low birth weight and residing in Baku and Nakhchivan. The mean age of the participants was 16.35 ± 0.06 years (range: 14–17 years). According to

the medical history data, all participants had been delivered at term but with low birth weight. The mean birth weight was $2,245 \pm 25.98$ g (range: 1,900–2,500 g). At the time of delivery, the mothers' mean age was 26.39 ± 0.13 years (range: 17–40 years). Among them, 28 women (43.1 %) were older than 35 years, while 8 women (12.3 %) were younger than 18 years.

Anthropometric assessment included measurements of height, body weight, arm span, lower limb length, biacromial shoulder width, chest circumference, and external pelvic dimensions.

In all menstruating participants, transabdominal pelvic ultrasonography was performed on the fifth day of the menstrual cycle using a Voluson S8 ultrasound system (South Korea). The obtained findings were compared with physiological parameters recorded in a control group of healthy adolescent girls ($n=30$).

Ultrasonographic Assessment and Statistical Analysis. The following ultrasonographic parameters were evaluated: uterine length, width, and anteroposterior diameter; length, width, thickness, and volume of both ovaries; endometrial thickness (M-echo).

Statistical analysis was performed using the Statgraph software package. Quantitative variables were assessed using methods of descriptive statistics. For each parameter, the mean value (M), standard error of the mean (SE), variance characteristics, and minimum and maximum values were calculated. Differences between groups were considered statistically significant at $p < 0.05$.

Results of the study. Physical Development of Girls Born with Low Birth Weight. Compared with healthy peers, girls in the study group demonstrated significantly lower values for body height, body weight, arm span, shoulder width, lower limb length, chest circumference, and external pelvic dimensions ($p < 0.05$). The anthropometric characteristics of girls born with low birth weight are presented in Table 1.

Table 1

Anthropometric characteristics of pubertal girls born with low birth weight (M $\pm$ SE)

Anthropometric parameters	Clinical groups		P
	Girls born with low birth weight (main) (n=65)	Practically healthy girls (control) (n=30)	
Height, cm	147 ± 0.11 (131–161)	157.8 ± 1.4 (143–168)	<0.05
Weight, kg	45.3 ± 0.31 (38–53)	56.4 ± 2.21 (46–72)	<0.05
Arm span, cm	149.3 ± 0.03 (136–157)	176.9 ± 1.13 (162–190)	<0.05
Shoulder width, cm	32.7 ± 0.08 (30–41)	39.6 ± 1.21 (32–46)	<0.05
Lower limb length, cm	76.8 ± 0.21 (70–91)	96.7 ± 2.1 (80–104)	<0.05
Chest circumference, cm	71.5 ± 0.9 (48–76)	96.2 ± 0.11 (88–105)	<0.05
Ferriman–Gallwey score	14.1 ± 0.08 (10–15)	8.3 ± 1.8 (6–10)	<0.05
External pelvic diameters, cm:			
– Dist. Spinarum	20.6 ± 0.31 (19–23)	24.8 ± 0.11 (22–26)	<0.05
– Dist. Cristarum	22.1 ± 0.19 (19–24)	26.2 ± 0.11 (23–28)	<0.05
– Dist. trochanterica	24.5 ± 0.09 (20–25)	29.9 ± 0.19 (27–30)	<0.05
– Conj. Externa	16.7 ± 0.29 (15–18)	20.2 ± 0.12 (18–22)	<0.05

Note: p – indicates statistical significance.

All anthropometric indicators in girls born with low birth weight were significantly reduced compared with healthy adolescents. In addition, the Ferriman–Gallwey score was significantly higher, indicating the presence of mild hirsutism in the study population.

Development of Secondary Sexual Characteristics. The assessment of pubertal maturation revealed significant differences between the groups. Assessment of secondary sexual characteristics revealed significant differences between girls born with low birth weight and healthy controls. The mean breast development (Ma) score was significantly lower in the low birth weight group than in the control group (1.1 ± 0.03 vs. 2.8 ± 0.02 , respectively; $p < 0.05$), indicating delayed mammary gland development. In contrast, axillary hair development was significantly more pronounced in girls born with low birth weight, with a mean Ax

score of 2.6 ± 0.09 compared with 2.0 ± 0.03 in the control group ($p < 0.05$). A similar pattern was observed for pubic hair development: the mean Pb score was significantly higher in the low birth weight group than in healthy controls (2.9 ± 0.10 vs. 2.0 ± 0.03 ; $p < 0.05$). Thus, girls born with low birth weight demonstrated a distinct pattern of pubertal development characterized by delayed breast development accompanied by relatively more advanced axillary and pubic hair development.

Girls born with low birth weight demonstrated significantly less advanced breast development compared with healthy controls. Conversely, axillary and pubic hair growth scores were significantly higher, suggesting a tendency toward relative hyperandrogenic manifestations during pubertal maturation ($p < 0.05$). Results of Ultrasonographic evaluation of the uterus and ovaries were assessed in girls born with low birth weight are presented in Table 2.

Table 2

Ultrasonographic parameters of the reproductive organs during puberty in girls born with low birth weight (M $\pm$ SE)

US-indices	Clinical groups		P
	Girls born with low birth weight (n=65)	Control group (n=30)	
Uterus			
Length, cm	3.6±0.11 (2.8–4.3)	7.1±0.11 (4.8–8.11)	<0.05
Width, cm	2.9±0.09 (2–4.9)	6.0±0.13 (3.0–7.11)	<0.05
Thickness, cm	2.6±0.09 (1.1–5.6)	4.2±0.21 (3.2–5.6)	<0.05
M-echo, cm	0.2±0.01 (0.1–1.6)	0.51±0.1 (0.2–1.3)	<0.05
Right ovary			
Length, cm	1.96±0.21 (1.2–3.6)	3.32±0.06 (2.5–4.1)	<0.05
Width, cm	1.6±0.03 (1.2–3.8)	2.3±0.06 (1.4–3.2)	<0.05
Thickness, cm	1.9±0.03 (1.1–2.9)	2.2±0.01 (1.6–3.0)	<0.05
Volume, cm ³	3.0±0.02 (1.6–17.9)	8.4±0.03 (6–18)	<0.05
Left ovary			
Length, cm	1.9±0.06 (1.0–2.9)	3.21±0.02 (2.1–6.1)	<0.05
Width, cm	1.63±0.06 (0.9–3.6)	2.6±0.08 (1.6–3.9)	<0.05
Thickness, cm	1.42±0.06 (1.2–2.6)	2.3±0.02 (1.6–3.8)	<0.05
Volume, cm ³	2.2±0.03 (1.1–15.0)	9.6±0.03 (6–20)	<0.05

Note: p – indicates statistical significance.

Thus, girls born with low birth weight demonstrated significantly lower ultrasonographic measurements of the uterus and both ovaries during puberty compared with healthy age-matched controls ($p < 0.05$).

Specifically, uterine dimensions, including length, width, anteroposterior diameter, and endometrial thickness (M-echo), were significantly reduced in the low birth weight group. Similarly, all measured parameters of the right and left ovaries, including length, width, thickness, and ovarian volume, were significantly lower than those observed in the control group ($p < 0.05$).

These findings indicate delayed development of the internal reproductive organs during puberty in

girls with a history of low birth weight and suggest that impaired intrauterine growth may have long-term consequences for reproductive system maturation.

The present study demonstrates that low birth weight is associated with significant alterations in physical growth, sexual maturation, and reproductive organ development during adolescence. Girls born with low birth weight showed lower anthropometric indices, delayed breast development, relatively more pronounced androgen-dependent hair growth, and reduced ultrasonographic dimensions of the uterus and ovaries compared with healthy peers.

Discussion. These findings are consistent with the developmental-programming concept, according to which adverse intrauterine conditions can induce

persistent structural, metabolic, endocrine, and epigenetic adaptations. International guidance on children born small for gestational age emphasizes that the consequences of impaired fetal growth may extend from infancy into early adulthood and include altered growth and metabolic and endocrine outcomes [4]. Contemporary reviews similarly describe the intrauterine environment as an important determinant of childhood and adolescent metabolic health [6]. Epigenetic studies provide an additional biological framework: Kuzawa et al. (2022) associated birth weight and maternal energy status with epigenetic age acceleration in young adults [7]. Quinn et al. (2023) reported an association between low birth weight and epigenetic age acceleration during early childhood [12].

The anthropometric findings in our cohort, including lower height, body weight, chest circumference, shoulder width, and pelvic dimensions, suggest incomplete postnatal catch-up growth. This interpretation is supported by the broader literature on fetal growth restriction. Nardoza et al. (2017) described fetal growth restriction as a condition with consequences extending beyond the prenatal period, and Sharma et al. (2016) summarized its antenatal and postnatal implications [9, 13]. Tang et al. (2017) also emphasized the multifactorial nature of fetal growth restriction and its potential long-term consequences [16].

A particularly important observation was the altered pattern of secondary sexual development: breast maturation was delayed, whereas axillary and pubic hair scores and the Ferriman–Gallwey score were higher. Recent studies indicate that prenatal and early postnatal growth can influence pubertal timing. Aghaee et al. (2022) demonstrated associations between infant growth and pubertal onset in girls [1]. Hvidt et al. (2019) likewise reported relationships between size at birth, infant growth, and age at pubertal development [5]. More recent data from Blaauwendraad et al. (2025) support associations of fetal and infant growth with pubertal timing [2]. In their work, Deng et al. (2025) showed that birth weight and prepubertal growth trajectory may have a combined effect on pubertal initiation in girls [3]. These observations suggest that pubertal development after low birth weight should be interpreted in the context of both prenatal growth and subsequent growth trajectories.

The increased androgen-dependent hair growth observed in our study may also be relevant to later endocrine health. Talarico et al. (2023) reviewed endocrine and metabolic disorders among adolescents and adults born small for gestational age and highlighted the need for continued surveillance beyond childhood [15]. Paalanen et al. (2021), studying young women born preterm, evaluated clinical and biochemical signs of polycystic ovary syndrome and provided evidence that adverse early-life conditions may be associated with later hyperandrogenic and metabolic phenotypes [10]. Although prematurity and low birth weight are not equivalent exposures, these findings support further investigation of androgen status in girls with impaired fetal growth.

The ultrasonographic findings provide additional evidence of delayed reproductive maturation. Reduced uterine dimensions, endometrial thickness, and bilateral ovarian volumes may reflect delayed maturation of estrogen-dependent reproductive structures. Because our study was cross-sectional and did not include hormonal measurements, a direct endocrine mechanism cannot be established; nevertheless, the combination of delayed breast development and reduced internal genital dimensions warrants longitudinal observation. Metabolomic evidence also indicates that intrauterine growth restriction is associated with complex biological alterations that may persist beyond fetal life [11].

The long-term reproductive significance of these adolescent findings remains to be clarified. Liffner et al. (2026), in a population-based register study, examined reproductive outcomes among women born with low birth weight, preterm, or small for gestational age and demonstrated that early-life growth characteristics may be relevant to later reproductive outcomes [8]. At the same time, Sydsjö et al. (2019) found that women born with very low birth weight had menstrual cycle patterns, pregnancy rates, and hormone profiles comparable with women born at term [14]. These apparently differing observations indicate that reproductive outcomes are heterogeneous and may depend on gestational age, severity of growth impairment, postnatal growth, and other modifying factors. From a clinical perspective, girls born with low birth weight may therefore benefit from longitudinal assessment of growth, pubertal progression, menstrual function, and, when indicated, endocrine and ultrasonographic parameters [4, 8, 15].

Conclusions

1. Girls born with low birth weight demonstrate significant delays in physical development during puberty, characterized by lower anthropometric parameters and reduced external pelvic dimensions compared with healthy peers ($p < 0.05$).
2. Pubertal development in girls born with low birth weight is characterized by delayed breast development accompanied by increased androgen-dependent hair growth and higher Ferriman–Gallwey scores ($p < 0.05$).

3. Ultrasonographic examination reveals significantly reduced uterine and ovarian dimensions, indicating delayed development of the reproductive organs ($p < 0.05$).

4. Low birth weight is associated with delayed sexual maturation manifested by impaired physical development, delayed secondary sexual characteristics, and reduced ultrasonographic indicators of reproductive organ growth.

References

1. Aghaee S, Quesenberry CP Jr, Deardorff J, Kushi LH, Greenspan LC, Ferrara A, et al. Associations between infant growth and pubertal onset timing in a multiethnic prospective cohort of girls. *BMC Pediatr*. 2022 Mar 31;22(1):171. doi: 10.1186/s12887-022-03242-0.
2. Blaauwendraad S, Gaillard R, Gonçalves R, Rivadeneira F, Dohle G, Oei E, et al. Associations of fetal and infant growth with pubertal timing. *Arch Dis Child*. 2025 Jun 19;110(7):539-544. doi: 10.1136/archdischild-2024-327060.
3. Deng R, Li W, Feng T, Wei L, Li X, Leng J, et al. Birth weight and prepubertal growth trajectory had a combined effect on pubertal initiation in girls. *Acta Paediatr*. 2025; 114: 1362–1370. <https://doi.org/10.1111/apa.17578>
4. Hokken-Koelega ACS, van der Steen M, Boguszewski MCS, Cianfarani S, Dahlgren J, Horikawa R, et al. International Consensus Guideline on Small for Gestational Age: Etiology and Management From Infancy to Early Adulthood. *Endocr Rev*. 2023 May 8;44(3):539-565. doi: 10.1210/endrev/bnad002.
5. Hvidt JJ, Brix N, Ernst A, Lauridsen LLB, Ramlau-Hansen CH. Size at birth, infant growth, and age at pubertal development in boys and girls. *Clin Epidemiol*. 2019;11:873. doi: 10.2147/CLEP.S217388.
6. Kardelen AD, Darendeliler F. The Role of the Intrauterine Environment in Shaping Childhood and Adolescence Metabolic Outcomes. *Metabolites*. 2025 Apr 6;15(4):252. doi: 10.3390/metabo15040252.
7. Kuzawa CW, Ryan CP, Adair LS, Lee NR, Carba DB, MacIsaac JL, et al. Birth weight and maternal energy status during pregnancy as predictors of epigenetic age acceleration in young adults from metropolitan Cebu, Philippines. *Epigenetics*. 2022 Nov;17(11):1535-1545. doi: 10.1080/15592294.2022.2070105.
8. Liffner S, Möller L, Bladh M, Nedstrand E. Reproductive Outcomes in Women Born With Low Birth Weight, Preterm or Small for Gestational Age: A Population-Based Register Study. *BJOG*. 2026 Jan;133(1):165-177. doi: 10.1111/1471-0528.18350.
9. Nardoza LM, Caetano AC, Zamarian AC, Mazzola JB, Silva CP, Marçal VM, et al. Fetal growth restriction: current knowledge. *Arch Gynecol Obstet*. 2017 May;295(5):1061-1077. doi: 10.1007/s00404-017-4341-9.
10. Paalanne M, Väärasmäki M, Mustaniemi S, Tikanmäki M, Wehkalampi K, Matinoli HM, et al. Clinical and biochemical signs of polycystic ovary syndrome in young women born preterm. *Eur J Endocrinol*. 2021 Jul 1;185(2):279-288. doi: 10.1530/EJE-20-1462.
11. Priante E, Verlato G, Giordano G, Stocchero M, Visentin S, Mardegan V, et al. Intrauterine Growth Restriction: New Insight from the Metabolomic Approach. *Metabolites*. 2019 Nov 6;9(11):267. doi: 10.3390/metabo9110267.
12. Quinn EB, Hsiao CJ, Maisha FM, Mulligan CJ. Low birthweight is associated with epigenetic age acceleration in the first 3 years of life. *Evol Med Public Health*. 2023 Jun 30;11(1):251-261. doi: 10.1093/emph/eoad019.
13. Sharma D, Shastri S, Sharma P. Intrauterine Growth Restriction: Antenatal and Postnatal Aspects. *Clin Med Insights Pediatr*. 2016 Jul 14;10:67-83. doi: 10.4137/CMPed.S40070.
14. Sydsjö G, Törnblom P, Gäddlin PO, Finnström O, Leijon I, Nelson N, et al. Women born with very low birth weight have similar menstrual cycle pattern, pregnancy rates and hormone profiles compared with women born at term. *BMC Womens Health*. 2019 Apr 25;19(1):56. doi: 10.1186/s12905-019-0753-y.
15. Talarico V, Nicoletti A, Raiola G. Endocrine and metabolic disorders in adolescent and adult patients born small for gestational age. *Acta Biomed*. 2023 Dec 5;94(6):e2023220. doi: 10.23750/abm.v94i6.15428.
16. Tang L, He G, Liu X, Xu W. Progress in the understanding of the etiology and predictability of fetal growth restriction. *Reproduction*. 2017 Jun;153(6):R227-R240. doi: 10.1530/REP-16-0287.

Conflict of interest. The authors have no conflicts of interest to declare.

ORCID: Mustafayeva I.R. <https://orcid.org/0000-0002-6854-6363>, Aliyeva E.M. <https://orcid.org/0000-0002-5459-1411>, Garashova M.A. <https://orcid.org/0000-0003-4805-7228>.

Article received: 22.07.2025