

# The impact of birth weight and maternal history on acne, hirsutism, and menstrual disorder symptoms in Turkish adolescent girls

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**Abstract** The aim of the study was to determine the association between birthweight, maternal medical history and acne, hirsutism, and menstrual disorder symptoms in Turkish adolescent population. Self-administered questionnaires were distributed to all volunteer female students at 15 secondary schools. The subjects' body mass index, birthweight, age at menarche, pattern of menstrual cycle, and presence of acne or hirsutism problems were recorded. Maternal obstetric parameters, menstrual cycle, presence of acne or hirsutism at present and at adolescent period were also asked. The impact of birthweight and maternal history on acne, hirsutism, and menstrual disorder symptoms was evaluated. The results of the study showed that after exclusion of subjects born prematurely, total of 1,309 students filled the questionnaires properly and included in the study. Of these students, 174 had low birthweight (LBW) (<2,500 g), 925 had appropriate (2,500–4,000 g), and 210 had high birthweight (>4,000 g). LBW students had higher incidence of menstrual disorder and acne problems ( $P = 0.032$  and  $P = 0.011$ , respectively). Maternal acne and hirsutism problems were significantly often in LBW group. Multivariate analysis showed that LBW was a predictor of acne, hirsutism, and menstrual

disorder at adolescent period ( $P = 0.001$ ;  $P = 0.01$ , and  $0.02$ , respectively). In addition, maternal menstrual disorder was also a predictor of menstrual disorder ( $P = 0.035$ ). We concluded that LBW is a good predictor of acne, hirsutism, and menstrual disorder problems in Turkish adolescent population.

**Keywords** Low birthweight · Acne · Hirsutism · Menstrual disorder · Maternal history

## Introduction

Polycystic ovary syndrome (PCOS) is a complex endocrine disorder with a prevalence of 5–10% of women at reproductive age [1] and characterized by acne, hirsutism, and menstrual disorder problems [2]. The etiology is not well clarified, but genetic and environmental factors appear to play an important role in its onset.

Beside genetic and environmental factors, recent studies showed that intrauterine reprogramming during suboptimal intrauterine conditions may cause several disorders arising later in life, such as cardiovascular disease, type 2 diabetes, obesity, hypertension, impaired ovarian development [3–11], and PCOS [12–15]. Intrauterine programming is known as early insults at critical stages of development lead to permanent changes in tissue structure and function. Birthweight has been considered as a major factor when investigating the etiology of adult-onset disease. Animal studies and human epidemiological data showed that this programming phenomenon occurs across the normal range of birthweight, with the worst prognoses at the extremes [16].

Previous studies have shown that family history PCOS symptoms are associated with clinical symptoms of

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patients with PCOS [17]. From this point of view, we aimed to determine the impact of birthweight on menstrual disorder, acne, and hirsutism symptoms in adolescent girls, as well as to evaluate whether there is an association between adolescent girls' symptoms and their mothers' menstrual cycle, acne, and hirsutism symptoms.

## Materials and methods

### Participants

Fifteen secondary schools were randomly selected. The selected schools had populations of 1,406 female students. Self-administered questionnaires were sent to all teachers and each teacher distributed the questionnaires to the female students in their classroom. 25 of 1,406 students did not give the questionnaire form to the director. 22 of 1,406 did not fulfill the form completely and excluded from the study. 1,359 students properly fulfilled the questionnaires and included in the study (Fig. 1). The study protocol was approved by the Local Ethical Committee and informed written consent was obtained from all subjects.

### Procedures

The questionnaire consists of the students' age, height, body weight, type of delivery, presence of prematurity, and birthweight. Age at menarche, pattern of menstrual cycle, and presence of acne or hirsutism problems were asked to all subjects. Presence of diabetes mellitus and hypertension in their parents or relatives were interrogated. Maternal

obstetric parameters such as age at delivery, smoking habitus, presence of obstetric complications including gestational diabetes mellitus, hypertension, and preterm delivery were also evaluated. Moreover, maternal menstrual cycle, presence of acne or hirsutism at present and at adolescent period was also noted.

### Statistical analysis

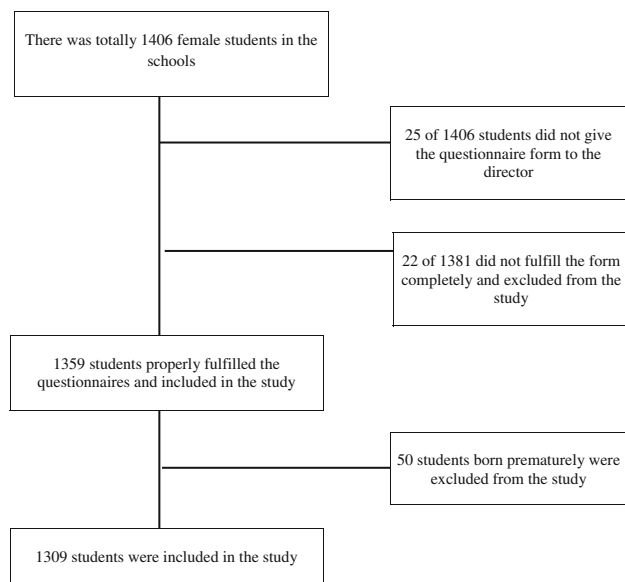
Data were analyzed with the SPSS software version 15.0 for Windows (SPSS Inc., Chicago, Illinois, USA). Data was transferred to computer media. Error control and necessary corrections were done. Groups were controlled in terms of conformity to normal distribution by graphical check and Shapiro–Wilk test. Median (range) was used for groups which was not distributed normally. Categorical variables are expressed as number and percentage. The Kruskal–Wallis test, followed by the Mann–Whitney test corrected with Bonferoni for multiple comparisons, was used for data that did not fulfill the assumptions required for analysis of variance. Chi-square tests were conducted to test the distribution between categorical variables. Logistic regression analysis was used to evaluate the value of maternal and fetal parameters to predict acne, hirsutism and menstrual disorder. *P* value of  $\leq 0.05$  was taken as significant. Power analysis of the study showed that 731 patients were needed to gain 80% power when alpha error was set at 0.05, beta error at 0.20, and effect size at 0.15.

## Results

Out of 1,381 questionnaires, 1,359 were properly filled, giving a response rate of 98%. Fifty students born prematurely (<37 gestational weeks) were excluded from the study. A total of 1,309 students' data were analyzed. The median ages of respondents and non-respondents were 16 years (range 13–20 years) and 15.5 (range 14–19 years). There was no statistically difference between respondents and non-respondents according to age and school type ( $P = 0.948$ ).

Median age at menarche was 13 years (range of 11–16 years). The median birth weight was 3,000 g (range 1,500–6,500). Median age of subjects' mothers was 41 years (range 31–58) and median age at delivery was 25 (16–40) years. BMI of girls and their mothers were 20 (14–33) and 27 (17–43), respectively.

One-thousand three hundred and nine female subjects, who were born with a birth weight <2,500 g were defined as group A, 2,500–4,000 g as group B, and >4,000 g as group C. There were 174, 925, and 210 girls in group A, group B, and group C, respectively. The baseline characteristics of all groups are summarized in Table 1. Birth



**Fig. 1** Recruitment flow chart of patients into study

**Table 1** Baseline characteristics of groups

Parameters	<2,500 Median (range)	2,500–4,000 Median (range)	>4,000 Median (range)	<i>P</i>
Age	16 (13–20)	16 (13–20)	16 (14–19)	0.342
Height	161 (145–173)	160 (140–175)	163 (150–175)	<0.001 <sup>a</sup>
Weight	49.5 (30–65)	51.5 (32–80)	56 (40–80)	<0.001 <sup>b</sup>
Age at menarche	14 (11–15)	13 (10–16)	13 (11–16)	0.002 <sup>a</sup>
Birthweight	2,000 (750–2,450)	3,000 (2,500–3,900)	4,400 (4,000–6,500)	<0.001 <sup>b</sup>
BMI	19.3 (14.0–27.0)	20.0 (14.6–30.9)	20.6 (15.4–33.8)	<0.001 <sup>b</sup>

<sup>a</sup> There is difference between group A and group C and group B and group C

<sup>b</sup> There is difference between all groups

weight, age at menarche, and BMI were significantly different (Table 1).

A total of 106 (8.1%) respondents reported various menstrual disorders. Oligomenorrhea was the commonest disorder and was reported by 78 (73.5%) of the respondents. This was followed by menorrhagia in 16 respondents (15.0%). Polymenorrhea occurred in only 11.3% of respondents.

Table 2 shows menstrual pattern, acne, hirsutism and delivery parameters of all groups. Menstrual disorder occurred in 31 (17.8%) girls in group A and in 25 (2.8%) girls in group B. The difference was statistically significant ( $P = 0.032$ ) (Table 2). Girls in group A had higher incidence of acne problems when compared to other groups ( $P = 0.011$ ). On the other hand, girls born with a birthweight of 2,500–4,000 g, had less hirsutism problems

( $P < 0.001$ ). Girls in group A significantly had higher rate of NICU admission when compared to other groups ( $P < 0.001$ ).

Obstetric and menstrual parameters of girls' mothers in all groups are shown in Table 3. Smoking was more common in group C than group B ( $P = 0.006$ ). History of acne and hirsutism problems in mothers was significantly often in group A when compared to other groups.

Two-step logistic regression analysis showed that the most important factor to predict acne formation was <2,500 g of birthweight of the girls ( $P = 0.001$ ). Furthermore, gestational hypertension and smoking were also important prognostic factors ( $P = 0.028$  and  $P = 0.049$ , respectively).

Three-step logistic regression analysis showed that low birthweight (LBW) was the only significant factor to

**Table 2** Menstrual pattern, acne, hirsutism, and delivery parameters of groups

Parameters	Group A ( <i>n</i> = 174) (<2,500 g)		Group B ( <i>n</i> = 925) (2,500–4,000 g)		Group C ( <i>n</i> = 210) (>4,000 g)		<i>P</i>
	<i>n</i>	%	<i>n</i>	%	<i>n</i>	%	
Menstrual disorder							
Yes	31	17.8	25	2.7	50	23.8	0.032 <sup>a</sup>
No	143	82.2	900	97.3	160	76.2	
Menstrual pattern							
Normal	168	96.6	836	90.4	199	94.7	<0.001 <sup>b</sup>
Oligomenorrhea	6	3.4	72	7.8	0	0.0	
Polymenorrhea	0	0.0	6	0.6	6	2.9	
Menorrhagia	0	0.0	11	1.2	5	2.4	
Acne							
Yes	41	23.5	156	16.9	25	11.9	0.011 <sup>c</sup>
No	133	76.5	769	83.1	185	88.1	
Hirsutism							
Yes	30	17.2	40	4.3	41	19.5	<0.001 <sup>d</sup>
No	144	82.8	885	95.7	169	80.5	
Delivery type							
Vaginal delivery	154	88.6	830	89.7	19	9.0	0.760
Cesarean section	20	11.4	95	10.3	191	91.0	
NICU admission							
Yes	65	37.4	27	2.9	0	0.0	<0.001 <sup>c</sup>
No	109	62.6	898	97.1	210	100.0	

<sup>a</sup> There is difference between group A and group B

<sup>b</sup> There is difference between all groups

<sup>c</sup> There is difference between group A and other groups

<sup>d</sup> There is difference between group B and other groups

**Table 3** Obstetric and menstrual parameters of girls' mothers in all groups

Parameters	Group A ( <i>n</i> = 174) (<2,500 g)		Group B ( <i>n</i> = 925) (2,500–4,000 g)		Group C ( <i>n</i> = 210) (>4,000 g)		<i>P</i>
	<i>n</i>	%	<i>n</i>	%	<i>n</i>	%	
Gestational hypertension							
Yes	20	11.5	60	6.5	5	2.4	0.002 <sup>a</sup>
No	154	88.5	865	93.5	205	97.6	
Age at delivery [median (range)]	23 (17–37)		25 (17–40)		25 (16–35)		<0.001 <sup>b</sup>
Gestational DM							
Yes	0	0.0	0	0.0	5	2.4	<0.001 <sup>c</sup>
No	174	100.0	925	100.0	205	97.6	
Smoking							
Yes	20	11.5	85	9.2	35	16.7	0.006 <sup>d</sup>
No	154	88.5	840	90.8	175	83.3	
Menstrual disorder at present							
Yes	11	6.3	31	3.3	10	4.8	0.269
No	45	25.7	685	74.1	150	71.4	
Menopause	118	68.0	209	22.6	50	23.8	
Menstrual disorder in adolescent period							
Yes	15	8.6	101	10.9	31	14.7	0.153
No	159	91.4	824	89.1	179	85.3	
Acne							
Yes	20	11.5	65	7.0	0	0.0	<0.001 <sup>a</sup>
No	154	88.5	860	93.0	210	100.0	
Hirsutism							
Yes	20	11.5	65	7.0	5	2.4	0.002 <sup>a</sup>
No	154	88.5	860	93.0	205	97.6	

<sup>a</sup> There is difference between all groups

<sup>b</sup> There is difference between group A and group B

<sup>c</sup> There is difference between group C and other groups

<sup>d</sup> There is difference between group B and group C

predict hirsutism in young girls ( $P = 0.01$ ). Other factors were not statistically significant.

Five-step logistic regression analysis showed that LBW, neonatal intensive care unit admission, and presence of menstrual disorder in mothers were important prognostic factors to predict menstrual disorder in girls ( $P = 0.021$ ;  $P < 0.001$ ; and  $P = 0.035$ , respectively).

## Discussion

PCOS is a common problem characterized by chronic anovulation, hyperandrogenism, and polycystic ovaries [2]. It is associated with metabolic abnormalities including insulin resistance, dyslipidemia, and increased risk for type 2 diabetes [18]. Many studies have been performed to understand the exact mechanism of PCOS.

Previous epidemiological, animal and clinical studies revealed that insults during the earliest stages of life can profoundly affect the health in adults and cause disease [19]. The differences in essential hypertension, diabetes, PCOS, and other diseases observed in certain ethnic groups

may not be due to only genetic predisposition, but may be rather the result of differences in the quality of the intra-uterine and postnatal environment.

Intrauterine reprogramming was considered to be responsible for the onset of PCOS. The possible association between LBW and later development of clinical and/or biochemical features of PCOS has been explored in few studies [12–17]; and conflicting results have been reported. In a study conducted by Melo et al., 165 women of which 43 were small for gestational age (SGA) and 122 appropriate for gestational age (AGA) underwent physical, laboratory and ultrasonographic examination. The prevalence of PCOS and hyperandrogenism was found higher in SGA group [20]. In another study, 35 LBW and 35 AGA women were compared with regard to clinical and biochemical markers of PCOS, and LBW was found to be at higher risk for developing PCOS features [21]. Similarly, Ibáñez et al. [13] reported higher androgen levels and lower birth weight than matched controls in girls with precocious pubarche and concluded that SGA girls tend to become hyperinsulinemic have central adiposity and have a reduced ovulation rate at adolescent period. In agreement

with previous studies, our results showed that LBW girls experienced significantly higher rate of menstrual disorder and acne problems compared to other groups.

On the other hand, some studies have found no relation between LBW and PCOS. In a French study, LBW was found to be associated with hyperinsulinemia, but not with higher androgens levels and higher prevalence of irregular menses [22]. However, in that study, LBW was defined as birthweight less than third percentile and the mean birthweight was higher than our study (2,500 g vs. 2,000 g). In another study, only 13 LBW women were included [23]. Furthermore, Ibáñez et al. [11, 24] reported that LBW-linked hyperandrogenism is associated with a reduced ovary volume with a low prevalence of PCOS. These conflicting results may be due to different selected study population and different definition of LBW and PCOS.

Previous studies showed higher prevalence of SGA newborns in PCOS mothers [15, 25]. The possible mechanism of this finding may be explained by insulin resistance and high levels of androgens in PCOS women [15]. Fetuses with monogenic disorders affecting insulin secretion or insulin sensitivity showed intrauterine growth retardation, which strongly supports the fetal insulin hypothesis [26, 27]. On the other hand, testosterone treatment during pregnancy caused fetal growth retardation in an animal study [28]. Supporting this data, our results showed that acne and hirsutism problems were significantly more frequent in mothers of LBW girls.

High birthweight have been reported as a factor in the etiology of PCOS, as well as impaired fetal growth [12]. However, we could not find a relation between high birthweight and acne, hirsutism and menstrual disorder symptoms.

In this study, age of menarche was higher in LBW group with respect to the other two groups and median menarche period was 3 years. Statistical analysis was performed whether this condition influenced menstrual disorder, acne and hirsutism formation but no difference was found between groups according to the period from first menarche. Therefore, menstrual disorder difference between groups was considered not to be related to menarche age.

Some limitations of this study include the diagnosis of PCOS could not be done according to ESHRE/ASRM Rotterdam criteria due to absence of biochemical and ultrasonographic evaluation. PCOS-related symptoms such as acne, hirsutism, and menstrual disorder were evaluated. The reliance on the subjects' memory was needed because records were based on anamnestic birth data.

As it is known, maternal history plays an important role in the etiology of PCOS [12]. To the best of our knowledge, none of the previous studies have evaluated the impact of birthweight and maternal medical history together. Strengths of the present study include maternal history

of PCOS-related symptoms (acne, hirsutism, and menstrual disorder) and birthweight data were analyzed together in multivariate analysis. In addition, in very few study both LBW and high birthweight were evaluated together [29]. Moreover, the sample size was larger than previous studies and this was the first study which has analyzed Turkish cohorts. The impact of LBW and high birthweight on acne, hirsutism, and menstrual disorder symptoms were evaluated together in this study. In rare study, it was evaluated together. Infants born prematurely were excluded to attribute the results only to LBW.

In conclusion, LBW (<2,500 g) was significantly related to self-reported PCOS symptoms (acne, hirsutism, and menstrual disorder) in Turkish adolescent population. Furthermore, maternal history of menstrual disorder was an another important prognostic factor to predict menstrual disorder.

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