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Menstrual irregularities, hormonal imbalance and obesity in adolescent girls in Hyderabad, Sindh, Pakistan: An observational study

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ORIGINAL STUDY

Menstrual Irregularities, Hormonal Imbalance and Obesity in Adolescent Girls in Hyderabad, Sindh, Pakistan: An Observational Study

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Abstract

Background: **Obesity in young girls adversely affects reproductive health later in life and it is a serious public health issue. The objective was to study the association of obesity with menstrual irregularities and hormonal imbalance in teenage and adolescent girls.**

Method: **Participants comprised a convenience sample of 12−19 years old girls (N = 83). The study was conducted in outpatient clinics at a university hospital. Data were collected through medical history by interview, physical examination and blood tests. Data were analysed using frequencies, descriptive statistics, Chi Squared tests of Independence and Binary Logistic Regression.**

Results: **The median age was 16 years (mean 15.9, SD 2.2) and the median BMI was 31.14 (mean 32.04, SD 4.51). Most of the girls were obese (95.2%) and some had a family history of obesity (33.7%), diabetes (28.9%) and cardiovascular disease (20.5%). Clinical presentations included secondary amenorrhea (34.9%), heavy and irregular periods (22.9%) and oligomenorrhea (16.9%). Girls with a polycystic ovary (54.2%, n = 45) had a reversed follicle stimulating hormone (FSH) / luteinizing hormone (LH) ratio (OR 11.33, 95% CI 2.98, 43.04, $p < 0.001$), an upper limit or raised fasting insulin (OR 7.20, 95% CI 2.33, 22.22, $p < 0.001$), a raised testosterone (OR = 5.16, 95% CI 1.56, 17.11, $p = 0.007$ and a disturbed lipid profile (OR 5.67, 95% CI 1.72, 18.73, $p = 0.004$). Obesity was not statistically significantly associated with either polycystic ovary syndrome (PCOS) or any of the measured hormone levels.**

Conclusion: **Adolescent girls presenting with obesity, menstrual irregularities and hormonal imbalance may suggest manifestation of PCOS, which needs early investigation and proper management.**

Keywords: Adolescent gynaecology, Child obesity, Endocrine disorders, Polycystic ovary syndrome, Reproductive health, Teenage obesity

1. Introduction

Obesity is a chronic non-communicable disease that is increasing not only in adults but also in adolescents especially females and it has become an epidemic in many low, middle and high income countries [1].

Obesity is associated with hormonal changes [2]. Obesity is also linked to polycystic ovary syndrome (PCOS), which is a hormone disorder of unknown aetiology; however, genetic, endocrine, environmental and behavioural factors play a role in it [3]. PCOS is mostly prevalent in adult women but commonly appears at puberty. PCOS is higher in South Asian women including 52% in women in Pakistan [4] where the prevalence of PCOS in adolescent girls is between 9% and 17% [5]. The main clinical features of PCOS include irregular

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menstruation, ovaries containing multiple fluid filled sacs (polycystic ovaries), obesity and hormonal imbalance such as raised levels of male hormones which manifests as oligomenorrhea (infrequent and scanty periods), hirsutism (excessive body hair) and acne [3]. PCOS in adolescent girls is also reported as more likely to be associated with obesity, anxiety, depression [6] and low self-esteem [7].

Childhood obesity is a major public health issue because it can adversely affect reproductive health in later life [8]. Obesity in young people is associated with behavioural and mental health problems [6,7], could lead to co-morbidities in adulthood and reduce life expectancy [9]. In addition, adolescent girls with obesity are more likely to have gynaecologic problems such as reproductive dysfunctions, alterations in menstruation, sterility and infertility [10]. Hence, obesity is a serious cause for concern for adolescent girls especially during this transitional stage of their physical, sexual and cognitive development [11].

More than half of the global obese population live in ten countries of which eight are lower and middle income countries [12] that include Pakistan, which is the fifth most populous country in the world. In Pakistan, about 49% of the total population are female and about 11% comprise teenage girls [13]. Obesity in Pakistan is projected to increase by about 156% and involve around 13.3 million people in 2040 compared to 5.2 million people in 2016 [14]. The country provides an opportune setting for the study of obesity which is higher in females than males in the country. In addition, there is a dearth of research on female obesity and gynaecological problems including menstrual disorders and hormonal disturbance especially in adolescent girls [15]. While there are very few studies on obesity and PCOS in adolescents girls in Pakistan [5,16], some of these studies have serious methodological limitations including the inappropriate use of BMI criteria for adults for determining obesity in teenage girls [16].

The primary objective of this research study was to study the association of obesity with menstrual irregularities and hormonal imbalance. The secondary objective was to identify significant environmental, lifestyle, behavioural and familial risk factors for obesity in adolescent girls.

2. Methodology

This cross-sectional observational study was undertaken in obstetrics and gynaecology outpatients clinics in a university hospital in Pakistan. The sample size was estimated by empirical way with the prevalence of obesity i.e. 5.5% in 10–19 years old girls in Pakistan [15] by applying the formula:

$$N = \left(Z^2 \times p \times (1-p)\right) / e^2$$

$$N = \left(1.96^2 \times 0.055 \times (1-0.055)\right) / 0.05^2$$

Where N = population/sample size, Z = 1.96 for a confidence level (α) of 95%, p = proportion of the total population (expressed as a decimal) for which we used 5.5% prevalence of obesity in Pakistani girls aged 10–19 years [15], and e = margin of error or confidence interval i.e. 5%, expressed as a decimal. Our calculated sample size was 80 girls and we added three more girls to compensate for estimated 4% dropout of participants from the study. Thus, our final sample size was 83 girls.

All 12–19-year-old girls who had menstrual problems and were either overweight or obese were invited to participate in this study. We recruited 83 girls using the simple random sampling technique.

Data were collected through medical history (by interview), physical examination, blood tests and ultrasound scan of the pelvic area. While taking medical history, we asked questions to participants about their age, menstrual problems, genetic/familial diseases (i.e. obesity, diabetes, and cardiovascular disease), lifestyle/environmental factors (i.e. dietary habits, intake of fast food, physical exercise, and sleeping and study hours) and behavioural factors (i.e. use of computers and mobile phones, playing outdoor games and watching TV).

Anthropometric measurements of height, weight and waist circumference were taken during the physical examination. Data on height and weight were used for calculating the body mass index (BMI), using the formula:

$$BMI = \frac{(\text{Weight in kg})}{(\text{Height in m})^2}$$

Obesity was determined by using age and sex specific BMI 95th percentile criteria [17]. Based on BMI-for-age percentiles criteria, weight is categorized as: underweight = BMI value less than 5th percentile; normal or healthy weight = BMI value from 5th percentile to less than 85th percentile (i.e. from 5th percentile to 84.9th percentile); overweight = BMI value from 85th percentile to less than 95th percentile (i.e. from 85th percentile to 94.9th percentile) and obese = BMI value at 95th percentile and greater [17]. Based on the above BMI percentile criteria, obesity was determined using the WHO BMI-for-age GIRLS 5–19 years (percentiles) expanded tables [18]. These tables provide WHO reference values for BMI by age in months starting

from age 5 (61 months) to 19 years (228 months) and BMI values for different percentiles (P) starting from P.01, P1, P2, P3, P5, P10, P15, P25, P50, P75, P85, P90, P95, P97, P99 and P99.9 [18]. Using the WHO BMI reference percentile values by age for girls, we assigned each participant a specific percentile based on their BMI values. If the BMI of any participant was between values of two percentiles given in the WHO reference tables [18], we assigned the mid-point between the two percentiles. For example, BMI of 24 for a girl aged 19 falls between the 75th percentile (BMI value 23.707) and the 85th percentile (BMI value 25.113) in the WHO BMI-for-age GIRLS 5–19 years (percentile) reference tables; we therefore assigned this BMI value the 80th percentile (P80), which is not given in the WHO reference table [18]. Using this process, we determined percentiles of BMI of all girls and then categorised their weight as normal, overweight or obese using the above mentioned BMI percentile criteria [17].

Blood tests provided data on hormone levels, which included follicle stimulating hormone (FSH) and luteinizing hormone (LH) ratio (FSH/LH Ratio), fasting insulin, testosterone, thyroid stimulating hormone (TSH), and lipid profile. Finally, trans-abdominal ultrasound scan of the pelvic area was done to examine presence of an ovarian cyst and polycystic ovaries.

The data were analysed by frequencies, descriptive statistics and Chi–Square Test for Independence when the expected frequencies in all groups were equal to or greater than 5. Fisher's Exact Test was used if more than 20% of the cells had an expected count or frequency of less than 5. Variables showing significant differences in the Chi Squared Test for Independence for the presence of obesity as well as polycystic ovary were included in binary logistic regression models, using the 'enter' method and criteria = P in (0.05) and P out (0.10). Results of binary logistic regression were expressed as odds ratio (OR) and 95% Confidence Interval (CI). A p value of <0.05 (Two-tailed) was considered statistically significant. Data were analysed using IBM SPSS Statistics version 28.0 for Windows (Armonk, NY: IBM Corp.).

2.1. Ethical considerations

This study was approved by the Institutional Ethical Review Committee of Liaquat University of Medical and Health Sciences (No. LUMHS/REC/-721, Date: 26/11/2018). Before data collection, a written consent was obtained from all participant girls' parents or guardians who accompanied them during the clinical appointments.

3. Results

Participants' socio-demographic characteristics, BMI, lifestyle and behavioural habits, and history of genetic/familial diseases are presented in Table 1. The median age of the sample was 16 years (mean 15.9, SD 2.2) and BMI was between 28 and 48.61 (median 31.14, mean 32.04, SD 4.51). Most girls were obese, had irregular diets, slept for 9 hours or more daily, did no physical exercise, and played no outdoor games; some girls reported a family history of obesity, diabetes and cardiovascular disease (Table 1). Obesity was not associated with age, waist circumference, familial diseases, environmental, lifestyle or behavioural factors (Table 1).

The most frequent menstrual irregularities reported were secondary amenorrhea, heavy and irregular periods and oligomenorrhea (infrequent and scanty periods) (Table 2). None of these menstrual irregularities was statistically significantly associated with either obesity or polycystic ovaries (Table 2).

Polycystic ovaries were found in many girls (54.5%) while an ovarian cyst was found in some girls (14.5%) and none of these was statistically significantly associated with obesity (Table 3).

Many girls had reversed FSH/LH ratio and upper limit and raised fasting insulin (Table 3). However, most of the girls had normal levels of testosterone, TSH and lipids (Table 3). Polycystic ovaries were statistically significantly associated with reversed FSH/LH ratio, upper limit and raised fasting insulin, raised testosterone and disturbed lipid profile (Table 3). However, none of hormonal imbalances was statistically significantly associated with the presence of an ovarian cyst or obesity (Table 3).

Results of binary logistic regression showed that girls with polycystic ovaries were more likely to have reversed FSH/LH ratio (OR 11.33, 95% CI 2.98, 43.04, $p < 0.001$), raised or upper limit of fasting insulin (OR 7.20, 95% CI 2.33, 22.22, $p < 0.001$), raised testosterone level (OR = 5.16, 95% CI 1.56, 17.11, $p = 0.007$ and disturbed lipid profile (OR 5.67, 95% CI 1.72; 18.73, $p = 0.004$).

4. Discussion

We studied the association of obesity with menstrual irregularities and hormonal imbalance as well as environmental, lifestyle, behavioural and familial risk factors of obesity in 12–19 years old girls.

We found that girls had menstrual irregularities i.e. secondary amenorrhea, heavy and irregular periods and oligomenorrhea but none of these was statistically significantly associated with either obesity, polycystic ovaries or hormonal imbalance.

Table 1. Participants' sociodemographic characteristics, environmental, lifestyle and behavioural factors, and history of familial diseases (N = 83).

Sociodemographic characteristics	Count	Percentage	Obese		
			No	Yes	P value
Age					
12−14 years	25	30.1	0	25	0.208
15−16 years	23	27.7	2	21	
17−19 years	35	42.2	2	33	
BMI by percentile					
Healthy weight (5th - < 85th percentile)	1	1.2	1	0	†
Overweight (85th − <95 percentile)	2	3.6	3	0	
Obese (95th percentile and greater)	79	95.2	0	79	
Waist circumference					
Less than 31 cm	29	34.9	3	26′	0.120
31 cm and more	54	65.1	1	53	
Environmental and Lifestyle factors					
Dietary habits					
Regular	25	30.1	1	24	0.999
Irregular	58	69.9	3	55	
Intake of fast food					
Daily	22	26.5	1	21	0.987
Twice a week	18	21.7	1	17	
Once a week or month	43	51.8	2	41	
Physical exercise					
Yes	23	27.7	2	21	0.306
No	60	72.3	2	58	
Sleep					
Less than 9 hours	27	32.5	3	24	0.099
9 hours and more	56	67.5	1	55	
Study hours daily					
Less than 5 hours	50	60.2	3	47	0.999
5 hours and more	33	39.8	1	32	
Behavioural factors					
Using computers and mobile phones					
Yes	29	34.9	1	28	0.999
No	54	65.1	3	51	
Playing outdoor games					
Yes	10	12.0	0	10	0.999
No	73	80.0	4	69	
Watching TV					
Yes	22	26.5	0	22	0.569
No	61	73.5	4	57	
History of familial/genetic diseases/disorders					
Obesity					
Yes	28	33.7	2	26	0.600
No	55	66.3	2	53	
Diabetes					
Yes	24	28.9	0	24	0.318
No	59	71.1	4	55	
Cardiovascular disease					
Yes	17	20.5	1	16	0.999
No	66	79.5	3	63	

Note(s): † Statistical testing not appropriate; hence, it was not done.

Nonetheless, the presence of menstruation irregularities could result in difficulties in socio-psychological adaptability and behavioural problems in teenage girls [6,7]. Therefore, proper clinical investigation and management of menstrual irregularities in adolescent girls must be done at an early stage.

Our findings showed that girls with PCOS had significant hormonal imbalance i.e. reversed FSH/LH ratio, raised levels of fasting insulin and

Table 2. Menstrual irregularities in adolescent girls with obesity and polycystic ovaries (N = 83).

Menstrual irregularities	Count	%	Obese			Polycystic ovary		
			No	Yes	*P* value	Present	Absent	*P* value
Secondary amenorrhea					0.999			0.720
Yes	29	34.9	1	28		17	12	
No	54	65.1	3	51		28	26	
Heavy and irregular periods					0.999			0.142
Yes	19	22.9	1	18		7	12	
No	64	77.1	3	61		38	26	
Oligomenorrhea					0.999			0.261
Yes	14	16.9	0	14		10	4	
No	69	83.1	4	65		35	34	

testosterone, and disturbed lipid profile. PCOS in adolescent girls is associated with hormonal imbalance [3], anxiety and depression [6] and low self-esteem [7]; hence, PCOS in girls aged 12–19 years needs an early investigation and proper management. We also found that girls with PCOS and ovarian cysts were obese; however, obesity was not statistically significantly associated with PCOS, ovarian cyst and any of the hormones studied.

We also found that a higher proportion of girls having waist circumference of 31 cm and more were obese; however, there was no statistically significant difference in obesity in girls with a waist circumference either less or more than 31 cm (Table 1). In addition, we did not find any statistically significant association between obesity and lack of physical exercise, watching TV, using mobile phones and computers, and sleeping for 9 hours or more, which are known risk factors for obesity. However, a possible explanation could be that girls in our sample mostly belonged to poor families from rural areas and therefore they did not have access to (smart) mobile phones and the Internet.

Obesity is a major health risk factor at young ages including teenage because it could lead to comorbidities such as diabetes, cardiovascular disease, and even disability in adult life [19], affect reproductive

Table 3. Polycystic ovaries, ovarian cysts, hormonal assays and obesity in adolescent girls (N = 83).

Investigations	Count	Percentage	Obese			Polycystic ovary		
			No	Yes	*P* value	Present	Absent	*P* value
Transabdominal pelvic ultrasound scan								
Polycystic ovary					0.328			
Present	45	54.2	1	44				
Absent	38	45.8	3	35				
Ovarian cyst					0.999			<0.001
Present	12	14.5	0	12		0	12	
Absent	71	85.5	4	67		45	26	
Hormonal assays								
FSH/LH ratio					0.244			<0.001
Normal	20	24.1	2	18		3	17	
Reversed	63	75.9	2	61		42	21	
Insulin (Fasting)					0.072			<0.001
Normal	23	27.7	3	20		5	18	
Upper Limit	37	44.6	0	37		21	16	
Raised	23	27.7	1	22		19	4	
Testosterone					0.568			0.010
Normal	62	74.7	4	58		28	34	
Raised	21	25.3	0	21		17	4	
Thyroid stimulating hormone					0.999			0.887
Normal	66	79.5	3	63		35	31	
Raised	17	20.5	1	16		10	7	
Lipid profile					0.569			0.005
Normal	61	73.5	4	57		27	34	
Disturbed	22	26.5	0	22		18	4	

Note(s): FSH = Follicle-stimulating hormone, LH = Luteinizing hormone.

health [8] and reduce life expectancy [9]. Hence, reduction of childhood obesity is needed at an early age through health promoting lifestyle interventions such as facilitating increased physical activities, and behavioural strategies and therapies for weight control [20]. In addition, health education for raising awareness about gynaecological problems including menstrual irregularities and hormonal imbalance in adolescent girls with obesity is imperative.

From the methodological perspective, there are no Pakistan specific BMI-for-age and sex reference levels for determining obesity by percentile in children aged 5–19 years. We therefore used the WHO reference values for BMI-for-age GIRLS 5–19 years (percentiles) expanded tables [18] as well as the US Centre for Disease Control (CDC) online BMI Calculator for children and teens [21]. We found that the US CDC percentile criteria used higher BMI values for lower percentiles compared to the WHO BMI-for-age percentile criteria (Fig. 1). Consequently, there was a difference in the categorisation of BMI of seven girls (8.4% of the total sample), who were categorised as overweight according to the US CDC criteria and obese according to the WHO criteria. The difference between the WHO and the US CDC BMI-for-age percentiles is due to different cut-off values and different reference populations. These findings may suggest that the WHO BMI percentile reference values given in BMI-for-age GIRLS 5–19 years (percentiles) expanded tables [18] are more appropriate for determining obesity is South Asian girls such as Pakistani girls aged 12–19 years as reported in this study.

4.1. Study strengths and limitations

Strengths: First, this study provides empirical evidence on menstrual irregularities and hormonal imbalance in adolescent girls with obesity in a lower middle-income country setting i.e. Pakistan. The second strength of the study is that there was a statistically significant association between polycystic ovaries and hormonal imbalance (i.e. reversed FSH/LH ratio, raised fasting insulin and testosterone) and disturbed lipid profile in 12–19 years old girls. The third strength of the study is that there was no statistically significant association of obesity with menstrual irregularities, hormonal imbalance and the presence of polycystic ovaries or an ovarian cyst in girls aged 12–19 years. The fourth strength of this study is the use of age and sex specific BMI percentile criteria for determining obesity in adolescent girls [17]; some previous studies on PCOS and obesity in adolescents conducted in Pakistan used BMI categories for adults for determining obesity in adolescent girls [16], which is inappropriate. The final strength of this study is that the WHO BMI-for-age (percentile) reference values for categorising obesity in girls [18] is more appropriate for South Asian girls (such as 12–19 year old Pakistani girls in this study) compared to the US CDC percentile criteria [21], which considers higher BMI values for lower percentiles compared to the WHO percentile criteria for girls (Fig. 1).

Limitations: Findings and generalisability of this study may be limited due to convenience sampling and a relatively small sample size, which however

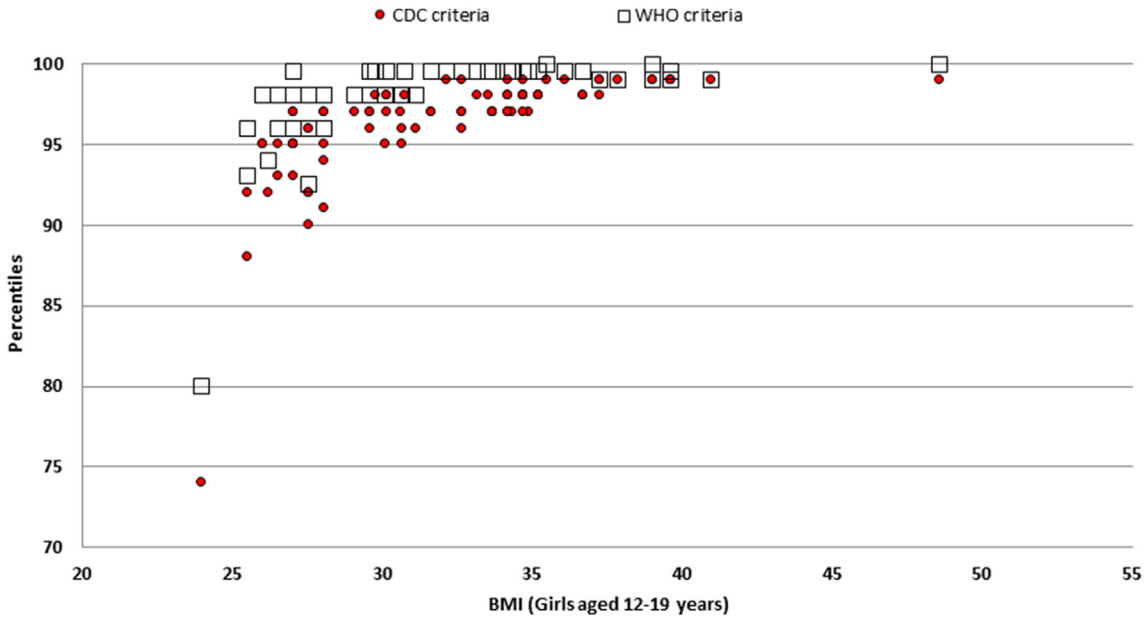

Fig. 1. BMI percentiles for girls aged 12–19 years according to World Health Organisation and the US Centre for Disease Control criteria.

was similar or higher to some very recent studies [7,16]. Another limitation of the study could be the use of the age of participants rounded in years as reported by their parents.

5. Conclusion

Adolescent girls with obesity presenting with menstrual irregularities and hormonal imbalance may suggest manifestation of PCOS, which needs early investigation and proper management. Obesity along with menstrual irregularities, hormonal imbalance and polycystic ovaries in 12–19 years old girls requires further research. WHO percentile criteria for BMI-for age GIRLS 5–19 years (percentiles) [18] are more appropriate for determining obesity in adolescent girls in Pakistan and other South Asian countries. The future research could develop Pakistan specific BMI-for-age 5–19 years (percentiles) for both girls and boys.

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Declaration of competing interest

The authors declared no conflict of interest.

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