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Research article

Circulating follicle stimulating hormone levels influence body growth in pre-menarcheal girls in a latitude-dependent manner

Amna Khalid [a], Rizwan Qaisar [b,c], M. Azhar Hussain [d,e], Asima Karim [b,f,*]

[a] Department of Family and Community Medicine and Behavioral Sciences, College of Medicine, University of Sharjah, Sharjah, United Arab Emirates
[b] Department of Basic Medical Sciences, College of Medicine, University of Sharjah, Sharjah, United Arab Emirates
[c] Cardiovascular Research Group, Research Institute for Medical and Health Sciences, University of Sharjah, Sharjah, United Arab Emirates
[d] Department of Finance and Economics, College of Business Administration, University of Sharjah, Sharjah, United Arab Emirates
[e] Department of Social Sciences and Business, Roskilde University, Roskilde, Denmark
[f] Department of Physiology & Cell Biology, University of Health Sciences, Lahore, Pakistan

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ABSTRACT

Introduction: Age at menarche is an essential determinant of reproductive life of a woman. Latitude is an important driver of age at menarche, however the contributions of circulating follicle stimulating hormone (FSH) and socio-economic status (SES) to age at menarche in a latitude-dependent manner is not known.
Methods: This population-based cross-sectional study is a component of our major cohort of 10,050 schoolgirls aged 8–16 years from 35 schools across 10 districts. The selected districts were categorised into high and low latitudes by applying a cut-off point at latitude 31.5°N. We evaluated the physical parameters, SES, circulating FSH, and growth hormone (GH) levels in premenarche girls (N = 252) at different latitudes.
Results: Self-reported age at menarche of girls residing at different latitudes in Pakistan showed that higher latitude is associated with delayed age at menarche. Higher latitude was associated with reduced circulating FSH levels, as well as lower parameters of physical growth including body mass index (BMI), waist-hip ratio and, waist-height ratio (all $p < 0.05$) in the premenarcheal girls. However, circulating GH levels were not affected by latitude. On the other hand, lower SES was associated with reduced GH levels and lower BMI, which are considered as probably the primary determinants of physical growth.
Conclusions: Taken together, we show that higher latitude may delay the sexual maturation, while poor SES may delay the physical growth in girls.

1. Background

Menarche is an important biological trait in the reproductive life of women and has several cultural, socio-economic, and epidemiological implications [1]. Several factors can influence the age of menarche. Among them, the socio-economic condition, genetic, nutrition, presence of disease, lifestyle, seasonal variations, and physical activities are increasingly being recognized as important determinants of the age at menarche [2,3].

* Corresponding author. Department of Basic Medical Sciences, College of Medicine, University of Sharjah, Sharjah, United Arab Emirates
E-mail address: akarim@sharjah.ac.ae (A. Karim).

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Abbreviations

FSH	Follicle stimulating hormone
GH	Growth hormone
BMI	Body mass index
WHR	Waist-hip-ratio
WHtR	Waist-height-ratio
SES	Socio-economic status

A north-south gradient is increasingly emerging as a possible driver of the age at menarche. The girl born at a lower latitude have a slightly earlier age at menarche than the girl born at high latitude [4]. While no exact explanation of this latitude-dependent variation in the age at menarche has so far been given, several candidates can, at least partially, account for this. For example, exposure to ultra-violet radiations (UVR) can accelerate the age at menarche. Lower latitude is typically associated with higher UVR and the girls born at this latitude reach the menarcheal age 3–4 months earlier than the women at higher latitude [4]. Similarly, there is evidence that the exposure to brighter light increases the circulating follicle stimulating hormone (FSH) levels, which can in turn lead to an earlier age at menarche [5]. This observation is consistent with longer day-length and brighter light at lower than higher latitudes. Further, the women born in summer months have an earlier age at menarche than those born in winter season [6].

A role for the activation of hypothalamus-pituitary axis (HPA) has been proposed in the earlier age at menarche at lower latitude. Higher socio-economic status (SES) can be associated with adequate nutrition, when compared to lower SES. Thus, the SES can influence the weight changes and body mass index (BMI), which seem to influence the age at menarche independent on the composition of diet [7]. SES is also shown to affect the circulating growth hormone (GH) levels, which is a prime determinant of physical health in the pre-menarche girls.

Studies investigating the mechanistic relation between latitude and the age at menarche vary substantially between different geographical localities, ethnicities, and the latitude degree [2,8]. These studies report considerable variations in the age at menarche, partly due to diversity in several factors such as genetics, latitude, SES, and climate, etc. [8]. Thus, there is a need to characterize the age at menarche in a relatively ethnically homogenous population with a comparable climate and small variations in the degrees of latitude.

We have recently shown that the age at menarche vary across schoolgirls in different population cohorts of Pakistan, where body growth parameters influence the age at menarche [9]. Here, we expand these findings by incorporating a novel dataset about the hormonal measurements and their relevance to the latitude and physical measurements in pre-menarcheal girls. This is partly because latitude may be a primary driver of age at menarche. To further characterize the effects of SES and latitude on the age at menarche, we collected data on the age at menarche in schoolgirls from Pakistan. The cohorts were divided into different subgroups based on latitude and SES levels. Since the circulating FSH and GH levels are partly driven by the latitude and SES, we investigated the correlation between the circulating levels of these two hormones and the age at menarche in a latitude- and SES-dependent manner. We hypothesized that the lower latitude could accelerate the onset of menarche by increasing the serum FSH levels, and this effect is independent of SES and GH levels.

2. Subjects and methods

2.1. Study participants

The present study design is cross sectional, performed from 2015 to 2017 and comprised schoolgirls (age range = 8–16 years) of Punjab. Since age of menarche varies enormously [10], 8 and 16 years have been reported to be the lowest and highest menarcheal ages respectively in Pakistan [11], therefore, we included these age ranges in our study. Punjab is the largest province covering around 200,000 km^2 (nearly 80,000 $miles^2$), highly populated with over 110 million people, distributed in 36 different districts. We selected 10 districts randomly based upon their latitude, topography, climate stretching from Murree district located in the north to Rahim-Yar-Khan district located in the south. The study participants represent around ~1% of the target population. The study was approved by the Ethical Review Committee (letter reference number UHS/ERB/22546/2014) of University of Health Sciences Lahore. An informed written consent was obtained from the participants and parents or legal guardians recruited in this study.

2.2. Sampling technique

A multistage cluster sampling technique was utilized to recruit the study participants. This study is a component of our major cohort comprising 10,050 schoolgirls from across the Punjab. The details of sampling technique are described elsewhere [12]. From this major cohort 5802 girls self-reported age at menarche and were included in the first part of analysis to see the effect of latitude on age at menarche. All the remaining estimates were determined on a subset of a sample including 252 pre-menarcheal girls. Briefly, the selected districts were categorised into low and high latitudes by considering Lahore as the cut-off point at latitude 31.5°N. Therefore, Sadiqabad, Rahim Yar Khan, Bahawalpur, D.G. Khan, Kasur, and Lahore were classified as being in the low latitude zone with a minimum latitude of 28.3°N. Sargodha, Gujrat, Rawalpindi, and Murree were categorised as being in the high-latitude zone with a maximum of 33.9°N (Table 1, upper part).

2.3. Data collection

We obtained the birth date of our schoolgirls from the school record. Then we calculated their ages from our sampling dates, exactly in days, month, and year. We then divided our participants into 9 groups (8–16 years) of 12-month age groupings. We recorded the data regarding onset of menstruation as a Yes/No in the questionnaire. The participants who answered yes were further asked to recall and report their age of menarche to the nearest one month. For the analysis, we rounded off to full years, as an example 10 years refers to girls with ages between 9.5 and 10.49 years. The socio-economic status (SES) defines a person's accessibility to various societal/ community resources [13]. We have categorised our schoolgirls by dividing them into middle and low class depending upon the standard of the school. We considered private schoolgirls as middle class and public schoolgirls as belonging to low class based upon the fact that tuition fees of private schools is very high as compared to public schools with almost free of cost education [14].

2.4. Anthropometric measurements

Anthropometric measurements of study participants were recorded based upon Centre for Disease Control (CDC) references for body weight, height, waist circumference (WC), and hip circumference (HC). We calculated BMI = weight (kgs)/height (m^2), waist hip ratio (WHR) = WC (cm)/HC (cm), and waist height ratio (WHtR) = WC (cm)/height (cm). Standardised methods and calibrated instruments were used for recording these measurements performed with due permission from the principal/dean of the participating school. The detailed methodology of the present study has been described elsewhere [12].

Table 1
Circulating hormone levels and physical parameters by district, latitude, and socio-economic status. Circulating FSH, GH levels, BMI, WHR, and WHtR of the pre-menarcheal girls (N = 252) according to latitude and SES. *$p < 0.05$, **$p < 0.01$, ***$p < 0.001$.

A. Summary statistics										
District	Statistics (Mean/Std. Dev.)	Latitude (Low/ High)	Latitude (Degrees North)	Circulating FSH (mIU/ml)	Circulating GH (mIU/ml)	BMI (kg/ m2)	WHR	WHtR	Age (years)	Sample size (N)
Sadiqabad	Mean	Low	28.3	5.69	17.2	16.2	0.768	0.359	10.6	7
	SD		0	1.90	20.4	1.4	0.059	0.021	0.9	
Rahim Yar Khan	Mean	Low	28.4	4.64	21.2	17.4	0.727	0.375	11.8	9
	SD		0	1.93	17.6	2.2	0.059	0.035	0.4	
Bahawalpur	Mean	Low	29.4	6.53	19.6	17.2	0.756	0.369	10.7	18
	SD		0	2.81	28.8	2.7	0.046	0.031	1.0	
D.G.Khan	Mean	Low	30.0	5.83	4.3	17.1	0.783	0.417	10.4	29
	SD		0	4.83	8.4	3.6	0.067	0.067	1.2	
Kasur	Mean	Low	31.1	7.77	12.4	16.7	0.765	0.384	11.1	11
	SD		0	4.15	11.2	1.8	0.044	0.027	0.6	
Lahore	Mean	Low	31.5	5.80	9.3	15.5	0.782	0.403	10.5	108
	SD		0	5.64	16.4	2.3	0.047	0.043	1.2	
Sargodha	Mean	High	32.1	7.00	16.1	17.7	0.734	0.393	11.7	12
	SD		0	3.58	18.8	2.4	0.068	0.047	0.5	
Gujrat	Mean	High	32.6	5.09	10.7	16.1	0.746	0.382	11.3	12
	SD		0	2.84	13.5	2.1	0.040	0.031	0.5	
Rawalpindi	Mean	High	33.6	3.46	19.3	17.3	0.768	0.394	10.2	17
	SD		0	2.53	15.5	4.2	0.039	0.049	1.4	
Murree	Mean	High	33.9	3.07	12.1	14.6	0.773	0.342	9.9	29
	SD		0	1.72	8.6	2.1	0.046	0.032	0.8	
Total	Mean		31.5	5.45	11.6	16.1	0.771	0.390	10.6	252
	SD		1.49	4.55	16.5	2.7	0.052	0.049	1.2	
B. Latitude and socio-economic status										
Latitude (degrees north):										
	Low			5.93	10.6	16.1	0.775	0.398		182
	High			4.18	14.3	16.1	0.76	0.37		70
	Difference			−1.75**	3.71	−0.1	−0.01*	−0.03***		252
	p value			0.001	0.075	0.872	0.037	0		
Socio-economic status:										
	Low			5.98	7.69	15.7	0.777	0.393		71
	Middle			5.23	13.17	16.3	0.769	0.389		181
	Difference			−0.75	5.47**	0.6	−0.01	0		252
	p value			0.366	0.009	0.061	0.249	0.543		

Notes: Follicle stimulating hormone, FSH; growth hormone, GH; body mass index, BMI; waist hip ratio, WHR; waist height ratio, WHtR.

2.5. Hormonal assays

Blood samples were drawn between 8 and 11 a.m. to determine serum hormonal levels. We collected the serum samples from schools in appropriate vacutainers, transported to the central lab in blood transport cooler boxes. Serum was separated, aliquots made and stored at −80 °C till further analysis. Serum FSH and hGH levels were determined in a sample of 252 pre-menarcheal girls by enzyme linked immunosorbent assay (ELISA) using commercially available kits (Monobind Inc, Lake Forest, CA, USA).

2.6. Statistical analysis

All data entry and analysis as well as graphs were performed using STATA version 12.0 [15]. In the regression analyses, the ordinary least squares (OLS) estimation approach was applied to find the magnitude and direction of influence of a given variable on the dependent variable [16]. We ignored the outliers with ± 4SD values and didn't consider them in further data analysis. We identified outlier values from z-score plots. To compare two groups with respect to different measurements, t-tests were applied. We considered

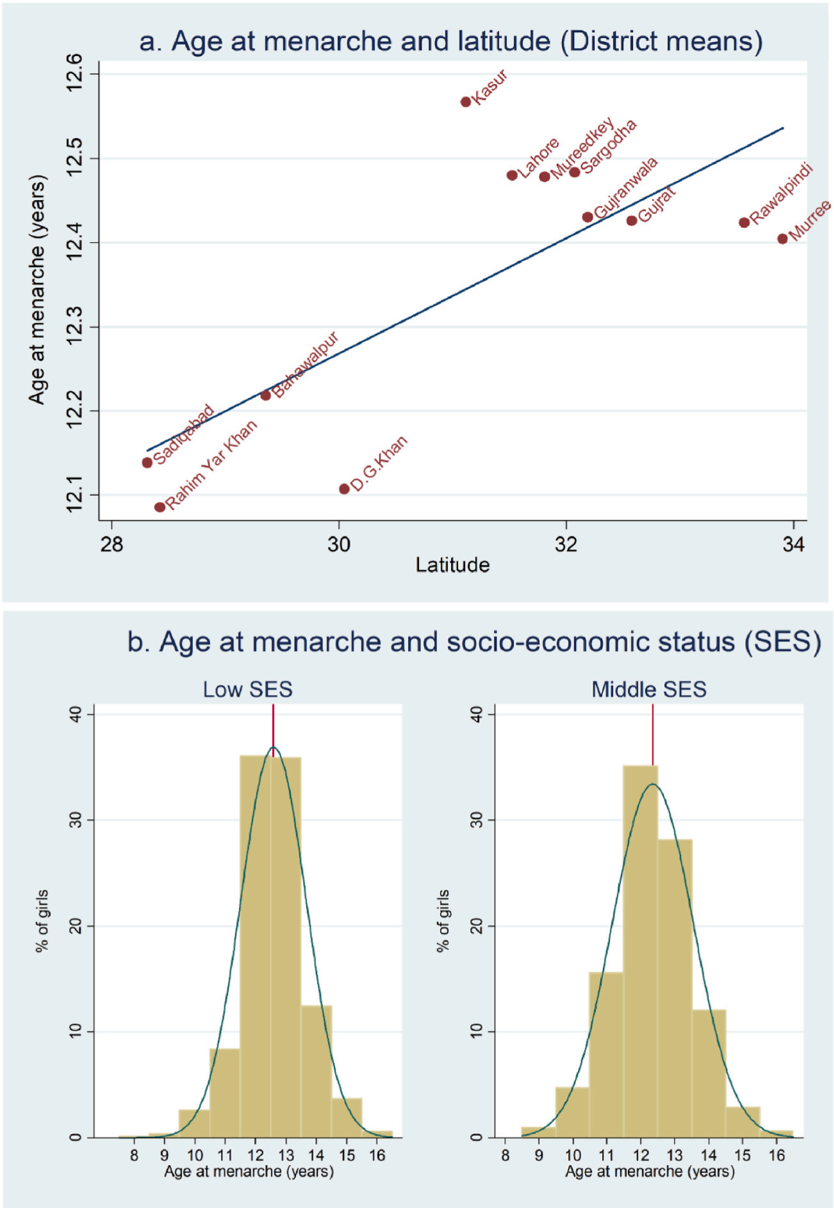

Fig. 1. Overall menarcheal age in the schoolgirls of Punjab (N = 5802) 8–16 years from (a) various districts based upon the latitude (north) and (b) SES. Vertical lines in the lower graphs represent the mean values.

statistically significant difference considering $p < 0.05$. * symbol showed a statistically significant difference based upon *t*-test analysis for the compared groups of participants. Various levels of significance with $p < 0.05$, 0.01, and 0.001 were shown by displaying *, **, *** symbols respectively.

3. Results

3.1. Means of central measures by district

Mean hormone levels and physical parameters are displayed in the upper part of Table 1. Since, the latitude (measured as degrees north) are at the district level, the results here are presented at the district level. The latitude varies from 28.3 (Sadiqabad) in the south to 33.9 (Murree) in the north. The average being 31.5, which is by chance also the location of Lahore. It is a measure of the north ward distance from equator. The FSH level (mIU/ml) has an average between 3.07 (Murree) and 7.77 (Kasur). The FSH seems to have a somewhat higher level in the southern cluster of districts, e.g., at low latitudes. In contrast, the northern cluster generally has a lower level of FSH, e.g., at high latitudes. The GH level (mIU/ml) does not show much of a clear pattern with respect to variation across latitudes. Its values across districts are between 4.3 (D.G. Khan) and 21.2 (R.Y. Khan). Any systematic pattern for the body mass index BMI (kgs/m^2) is also difficult to detect. The lowest mean is in Murree (14.6) while the highest mean (17.7) is in Sargodha. The WHR shows only little variation between the districts with the highest district (D.G. Khan) only 8% above the lowest district (R.Y. Khan). The WHtR shows much more variation with values between 0.342 (Murree) and 0.417 (D.G. Khan).

Generally, we see the greatest relative variation (percent district difference between maximum and minimum) for GH and FSH, while WHR has lowest variation, and latitude, BMI and WHtR have quite the same relative variation.

3.2. Age at menarche by latitude respectively SES

3.2.1. Latitude

The south-north clustering of districts is apparent from Fig. 1a that shows district means of age at menarche versus the latitude of the district. The relationship between latitude and age at menarche appears positive, which means the higher the latitude where the respondent is living, the higher the age of menarche, e.g., first menstruation is delayed the further north the girl's residence. The relationship is statistically significant, and it implies that age at menarche is 27 days higher when the latitude increases by 1°.

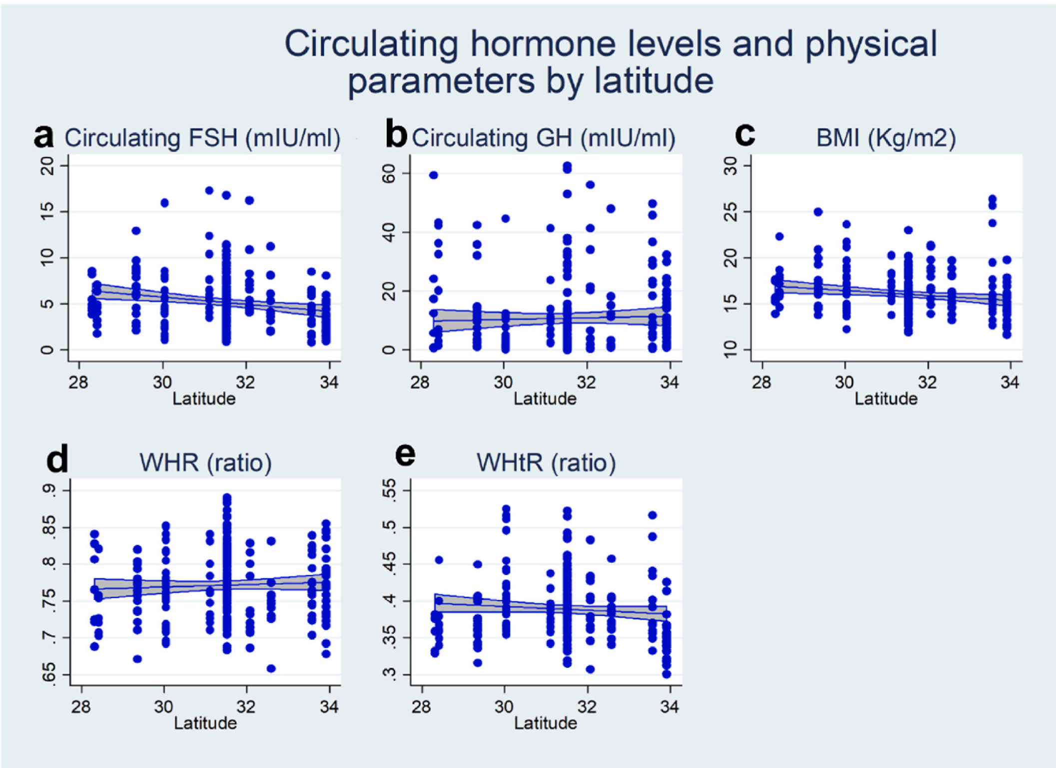

Fig. 2. Correlation of circulating FSH (a), GH (b) levels and physical growth parameters BMI (c), WHR (d), and WHtR (e) with latitude (north) in various districts of Punjab among pre-menarcheal girls aged 8–16 years (N = 252). The units for Y-axis are given in parenthesis in subheadings of each graph. Follicle stimulating hormone, FSH; growth hormone, GH; body mass index, BMI; waist hip ratio, WHR; waist height ration, WHtR.

3.2.2. SES

The socio-economic situation also seems to affect the age at menarche, but not to a large extent (Fig. 1b). For both groups we see a pretty much normal distribution of age at menarche. The mean age at menarche is slightly higher for girls with lower socio-economic background compared to girls with middle socio-economic background.

3.3. Latitude/socio-economics and hormone/physical measurement

3.3.1. Latitude

Higher latitude seems to be negatively associated with FSH as well as BMI (Fig. 2a and c), whereas there seems to be no effect on GH (Fig. 2b) and WHR (Fig. 2d). A closer investigation shows that mean FSH is 5.93 for girls in low latitude districts and 4.18 in high latitude districts, which is a difference of 1.75 that is statistically highly significant (Table 1, lower part). This means, that FSH is on average lower in girls living in high latitude places compared to girls living in low latitude places. Similarly, we also see that WHR and WHtR (Fig. 2e) is significantly lower for girls in high latitudes compared to girls in low latitudes (p value is respectively 0.037 and 0.0001). BMI is also lower, but this effect is not significant (p value of 0.872). Similarly, a positive effect of higher latitude recorded for GH is not statistically significant (p value is 0.075).

3.3.2. SES

SES is generally not important for hormone levels and physical measurements (Fig. 3a, c, d & e). An exception is GH (Fig. 3b), where we see that girls with low SES have a mean GH of 7.69, while girls with middle SES have a GH level of 13.17, which represents a difference of 5.47 (Table 1, lower part). This difference is statistically significant with a p value of 0.009, and thus higher socio-economic status is associated with higher GH levels.

3.4. Regression analysis

A more precise identification of the direction of any effects of latitude and SES and the magnitude of any possible effects is possible through regressions of levels and measurements (Table 2). We see a statistically significant negative effect of latitude on FSH ($p < 0.001$), BMI ($p < 0.01$), and WHtR ($p < 0.05$), while there is a statistically significant positive effect of middle SES on GH ($p < 0.01$),

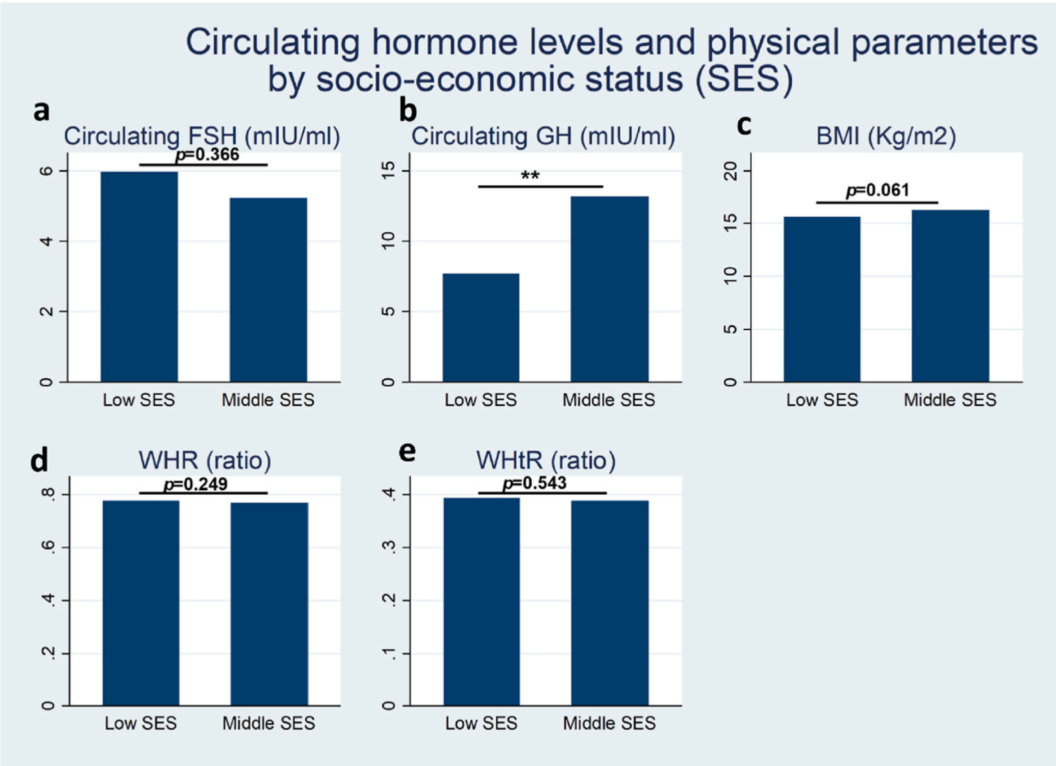

Fig. 3. Circulating FSH (a), GH (b) levels, and physical parameters of BMI (c), WHR (d), and WHtR (d) according to SES of pre-menarcheal girls aged 8–16 years (N = 252). Values are expressed as means, *$p < 0.05$, **$p < 0.01$, ***$p < 0.001$, middle vs. low SES. Units for Y-axis are given in parenthesis in subheadings of each graph. Follicle stimulating hormone, FSH; growth hormone, GH; body mass index, BMI; waist hip ratio, WHR; waist height ration, WHtR.

Table 2
Regression of hormone levels and physical parameters. Regression analysis of latitude and SES with circulating hormones levels and physical parameters in pre-menarcheal girls. Higher latitude was associated with significant reduction in circulating FSH levels, BMI, and WHtR. Middle SES was associated with higher circulating GH levels and BMI. Values in parenthesis are SE (standard error) of estimates. $*p < 0.05$, $**p < 0.01$, $***p < 0.001$.

	Circulating FSH (mIU/ml)	Circulating GH (mIU/ml)	BMI (kg/m^2)	WHR	WHtR
Latitude (degrees north)	−0.494*** (0.119)	−0.184 (0.728)	−0.325** (0.117)	0.002 (0.002)	−0.004* (0.002)
Middle socio-economic status	−0.703 (0.824)	5.491** (2.086)	0.648* (0.325)	−0.008 (0.007)	−0.003 (0.006)
Constant	21.486*** (3.751)	13.478 (22.865)	25.863*** (3.666)	0.725*** (0.070)	0.530*** (0.066)
R-squared	0.024	0.015	0.034	−0.001	0.012
N	252	252	252	252	252

and WHR is not significantly affected by either latitude ($p > 0.05$) or SES ($p > 0.05$).

More specifically, FSH is on average reduced by 0.494 mIU/ml when latitude increases by 1°. BMI goes down 0.325 kg/m^2 when latitude increases by 1°. Finally, a 1° increase in latitude is associated with a 0.004 points reduction in WHtR. Regarding SES, we see that the GH is 5.491 mIU/ml higher for girls with middle SES compared to girls with low SES.

4. Discussion

To our knowledge this is the first report describing an inverse association between latitude and the age at menarche in the Pakistani population. We have reported that body growth parameters influence the age at menarche in our cohort of schoolgirls and the delayed age at menarche is correlated with stunted body growth [9]. Previous reports show that in addition to physical growth, other factors such as geography (latitude, lighting hours) of the region influence age at menarche [17]. Here, we report that latitude influences age at menarche and FSH levels, but no or little effects on physical growth and GH levels. We show that the SES is one significant determinant of these two parameters independent of latitude. The girls living in districts with high latitude or low exposure to day light had 4–5 months of delay in menarche than the girls born in districts with low latitude or higher exposure to day light. We propose reduced FSH levels as a potential driving force behind delayed menarche.

The results are indicative that age at menarche is affected by changing latitudes. An association between latitude and age at menarche has been described previously but the role of hormonal interplay in driving this relation is elusive. Our findings suggest that lower FSH levels at higher latitude can be a possible mechanism delaying the onset of menarche. This can at least partly be explained by the reduced day length at higher latitude [17]. Latitude is correlated with FSH levels, however it is possible that factors other than latitude like nutrition, genetics, lifestyle, and physical activity are also affecting the FSH levels in pre-menarcheal girls [18,19]. Inadequate light exposure in the childhood for girls dwelling at high latitude regions can be a contributing factor for experiencing delayed menarche. Lower photoperiod (i.e., shorter day length) associated with high latitude can be one possible mechanism involved in delayed age at menarche [4]. Even exposure to artificial light for a longer period was observed to have a negative association with age at menarche [20].

High levels of melatonin in the pre-pubertal phases of life are associated with the inhibition of this reproductive axis. Melatonin levels are in turn associated with photoperiod/day length [21], as the photoperiod signals are encoded in the form of biochemical information through melatonin released from pineal gland, which is primarily active in darkness [22]. In our study the early activation of HPG axis can account for higher levels of circulating FSH levels at low latitude. This can be attributed to lower melatonin levels due to higher photoperiods and longer day length at low latitudes [23]. Our data suggest that at lower latitude, due to higher photoperiod/longer day lengths there may be lower levels of melatonin thereby stimulating GnRH release and in turn high levels of gonadotropins [24]. Moreover, studies conducted on hamsters and sheep show that the photoperiodic changes in kisspeptin levels are associated with changes in melatonin levels. This evidence suggests that melatonin has a potential link with kisspeptin-associated photoperiod variations, although the presence of melatonin receptors on kisspeptin neurons is still not established [25]. This is suggestive of a hypothesis that some intermediate pathway might be involved between photoperiod, melatonin, and kisspeptin, which affects the HPG axis stimulation and onset of menarche. Two potential pathways have been proposed in inducing delayed menarche at higher latitude by affecting HPA and melatonin levels. One possible mechanism can be that the high levels of melatonin at high latitudes with shorter day length can cause the release of RFRP-3, a member of RFamide peptide family, which inhibits GnRH [26]. The second proposed theory can be that high melatonin in short days may strengthen the negative feedback effect of sex steroids on kisspeptin expression, which keeps the HPG axis quiet as observed in hamsters [27,28].

We have recently determined the incidence of obesity and stunting among the schoolgirls in various districts of Punjab [29,30]. In the present study our results demonstrate a negative correlation of latitude with BMI and WHtR, which are known indicators of obesity and body fat distribution. These observations are consistent with previous studies and can partly be explained by the association between high latitude and high basal metabolic rate (BMR) [31]. Moreover, an inverse relationship has been proposed between high latitude and low ambient temperature. Therefore, at higher latitude in colder environment, one of the body's compensatory mechanism can be cold-induced thermogenesis to maintain the body temperature by increasing BMR [32]. In association with this phenomenon loss of appetite has also been evidenced among higher latitude dwellers. Additionally, another possible explanation of lower body fat accumulation amongst girls living at higher latitude can be the excessive physical activity leading to increased energy loss to combat with challenges faced due to the topography of those regions [33]. A certain amount of body fat is required in the females to initiate puberty as proposed by the critical weight hypothesis [34]. It is well known that leptin, a satiety hormone plays a role in the activation of HPG axis at puberty and the main source of leptin is body fats [35]. Therefore, it is possible that the pre-menarcheal girls at high latitude have less body fat stores with low levels of circulating leptin and delay in the onset of menarche as compared to the girls living at low latitude.

We have also reported that the SES affects the circulating GH levels and BMI in our pre-menarcheal schoolgirls, suggesting that girls with middle/high SES had higher levels of circulating GH and higher BMIs as compared to the girls with low SES. However, latitude had little or no effect on the GH levels in our cohort. Body growth of children with same age and ethnic group is markedly affected by the favourable SES conditions [36]. Although postnatal growth is largely affected by recurrent infection and chronic diseases, our study cohort were healthy girls with normal height and weight. Our results demonstrate that even amongst the healthy children height, weight (BMI), and circulating growth hormone levels can be affected by SES. These observations are highly suggestive of the importance of nutrition during these critical growth periods. Preadolescent girls belonging to disadvantaged households in terms of food and water provision, availability of health services, and sanitation, etc., suffer malnutrition as compared to those who belong to better-off houses [37].

The results from our study can help identify the effects of circulating FSH levels and SES on the age at menarche in a latitude-dependent manner. Pre-menarcheal girls residing in lower latitude zones have higher FSH levels and a trend of early menarche, which can have adverse effects on general health of this female population. Additionally, our data suggest the association of adiposity during the pre-menarcheal period with high SES leading to early sexual maturity. Therefore, health strategies should be designed and implemented accordingly to combat these challenges.

The major strength of the present study is that the population is rather homogenous ethnically and genetically, reducing/minimizing the effects of population genetics and ethnicities. Moreover, variations in latitude are small and can help dissect minute effects of varying latitude. The circulating FSH levels reported here are from the pre-menarcheal girls, so the variations in FSH levels due to the menstrual cycle is not a confounding factor here.

5. Limitations

The study was conducted in the province of Punjab only and does not account for inter province variations. Additionally, in low SES classes and in rural parts, mostly child births occur at places without healthcare services, which means the date of births may be inaccurately reported, especially for the participants studying in public sector schools. Since it was a cross-sectional study and we had a wide range of ages of schoolgirls, it was hard to minimize the recall interval while reporting the ages at menarche. It is possible that other potential confounders, such as diet, lifestyle, and racial backgrounds of the participants may affect the age at menarche. However, we are confident that the relatively homogenous racial and cultural backgrounds of participants minimize the potential effects of these confounders. The sample size of 252 is smaller than our previous studies with relevant data ([12]). However, this represents pre-menarcheal girls with homogenous ethical, socioeconomic, and cultural profiles, which builds our confidence in the biological significance of our data. Nevertheless, further studies are required to extend the characterization of factors affecting the interface between latitude and age at menarche.

6. Conclusions

There is a significant correlation of circulating FSH levels in pre-menarcheal girls with latitude, indicating late menarche in high latitude dwellers as compared to those living at low latitude. Additionally, we found a significant positive correlation of body fat especially visceral fat and circulating GH levels with SES, suggesting greater incidence of higher BMI among girls belonging to middle class as compared to those who belong to low SES. The outcomes of this study highlight the necessity for the development of approaches to prevent excessive weight gain among children belonging to better off families. Moreover, findings of the present study suggest that children living in high light exposure attain early maturation.

Author contribution statement

Amna Khalid; M. Azhar Hussain: Analyzed and interpreted the data; Contributed reagents, materials, analysis tools or data; Wrote the paper.

Rizwan Qaisar: Conceived and designed the experiments; Analyzed and interpreted the data; Contributed reagents, materials, analysis tools or data; Wrote the paper.

Asima Karim, Ph.D.: Conceived and designed the experiments; Performed the experiments; Analyzed and interpreted the data; Contributed reagents, materials, analysis tools or data; Wrote the paper.

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Data availability statement

Data will be made available on request.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.heliyon.2023.e15293.

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