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Assessment of age at menarche and its relation with body mass index in school girls of Riyadh, Saudi Arabia

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ABSTRACT

Aims and Objectives: Increase of childhood obesity prevalence and rapid changes in socio-economic status resulted in a decline in age at menarche, which contributes, to a number of diseases affecting women's future health. The objective of this study is to assess the mean age at menarche in girls of ages 9-16 and observe its relationship with their body mass index and other covariates in Riyadh, Saudi Arabia. **Materials and Methods:** A cross-sectional study was conducted among 304 female students of both private and governmental schools in Riyadh, Saudi Arabia, during March –May 2013. Data on demographics, socioeconomic status, physical activity, diet, and age at menarche were collected from students and their mothers, using self-administered questionnaires. Physical examinations were conducted to collect the anthropometric measurements. **Results:** Out of 304 students with a mean age (SD) of 12.52 (2.08), 165 (54.3%) attained menarche. Mean menarcheal age (SD) for the girls was 12.08 (1.28). The mother's mean age at menarche was positively correlated with their daughters ($r = 0.411$, $P < 0.001$). There was no significant correlation between BMI and age at menarche ($P > 0.05$). Governmental school students attained menarche at a higher age (12.34) than private school students (11.59), and the difference between them was statistically significant ($P < 0.001$). **Conclusion**: Schoolgirls in our study attained menarche at an early age with a mean menarcheal age of 12.08 years. Our data follows the globally and regionally observed declining trends of age at menarche. When assessing BMI as an influencing factor of onset of menarche, our results showed no correlation. Further longitudinal studies are encouraged to monitor factors influencing the onset of menstruation, in order to prevent the potentially adverse consequences of early menarche.

Key words: Menarche, Obesity, BMI, Saudi Arabia, Women health

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INTRODUCTION

Menarche, onset of menstrual period, is considered the most noteworthy event that chronicles the maturation of the female reproductive system. It is accepted within the scientific community, that the mean age at menarche is subjected to change depending on numerous factors; genetic and environmental predictors; such as nutritional status, and socioeconomic status.[1-4] A downward trend in the age at menarche has been reported globally over the past hundred years. Among the various factors, the most important determinants of age at menarche, is the growing epidemic of obesity.[5] Despite the increasing rates of childhood obesity and rapid changes in socio-economic status in the Gulf countries, due to the profound impact of oil-provoked modernization, the mean age at menarche and the repercussions of increased obesity rates on puberty remains mostly unknown among girls in Saudi Arabia.[6,7] The timing of early menarche has received considerable attention due to its association with women's future health.

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It is known to be an established risk factor for breast cancer, which has been the most common type of malignancy in Saudi females for the past 12 years.[8] In addition, it is a contributing factor to a number of diseases, including metabolic syndrome, type 2 diabetes, cardiovascular disease, mood disorders, and all cause-mortality.[9-12]

The present study was carried to assess age of menarche and its relation with body mass index, and other covariates such as anthropometric measures, mother's age at menarche, physical activity, dietary habits and socioeconomic status.

MATERIALS AND METHODS

A cross-sectional study was carried out in one private and three governmental schools according to grades (elementary, intermediate, and secondary) in Riyadh, Saudi Arabia, during March-May, 2013. Selection of our sample from private and governmental schools was to represent a widened variety of socioeconomic status.

The study population comprises students attending public and governmental schools from 4th to 10th grade, ages ranging from 9 to 16 years old. According to consulted experts, the initial changes of pubertal development commence 2 years prior to menarche. Thus, we choose 9 years old as the lower limit for our sample to avoid intertwining with the parameters of precocious puberty. As for choosing 16 as the upper limit, we included the possibility of delayed menarche in order to assess its significance in evaluating the association of BMI to menarche and to avert underestimation of the true age at menarche.

The schools were chosen conveniently in terms of feasibility and location; one private and three governmental schools (elementary, intermediate, and secondary). Within each of the schools, systematic sampling was applied. Depending on the number of students in each class, surveys were distributed to either every 5th or 3rd student off an attendance sheet. Incomplete questionnaires and reported diagnosed conditions, such as, hormone related disorders, diabetes, skeletal, neurologic or muscular disorders and those who were on any long-term medication, that could disrupt the natural occurrence of menarche, were excluded.

Due to cultural norms in the Middle East and the sensitivity of the topic, self-administered questionnaires were used rather than personal interviews.[13] The purpose of the study was explained to students and the teachers. No exchange of information transpired between the researchers and students to avoid selection bias. The survey was color-coded with a set of questions for the mother, and another set for the student. The questionnaire was both in English and Arabic.

Researchers and volunteers measured height, weight, waist and hip circumferences according to standard protocol. Height without shoes was measured to the nearest centimeter using a stadiometer (Detecto). Students were weighed wearing standard school uniforms to the nearest 0.1 kilogram using a scale (Detecto). Body mass index (BMI) was calculated as body weight in kilograms divided by height in squared meters. BMI-for-age was calculated by means of weight, height, age, and gender, as determined by the growth charts provided using Epi info 2002 CDC, US, software program published by the CDC.[14] Underweight was defined as less than or equal to 5th BMI percentile, while, overweight and obese were defined as more than or equal to 85th and 95th percentile, respectively. Accordingly, the normal was defined as between the range of more than 5th and less than 85th percentile. Waist and hip circumferences were measured according to the World Health Organization (WHO) recommendations. Waist and hip circumferences were measured with a stretch-resistant measuring tape. All measurements were in centimeters (cm) to the nearest 0.1 cm.

Sample size

Using the evidence from literature and assuming a minimum inverse correlation "r" value as 0.20 between menarcheal age and body mass index (BMI) among the students (by using Cohen(1988) tables for sample size required to detect a correlation at $\alpha = 0.05$ (level of significance) and power (1-β) of 0.80, 153 girls was estimated as the number needed. Since the age range of 9 to 16 was selected for our sample, students from grade 4 to grade 10 were chosen, and the sample size of 40 from each of these 7 levels was assumed for consideration in order to compensate for the wide range of the selected ages. As a result, the sample size was a total of 280 students. Anticipating a 30% non-response from the study subjects, the required sample size was 364 students.

Data was analyzed using IBM SPSS Statistics Software Version 21. Participants' characteristics were described using frequencies. Age at menarche for both mothers and daughters and BMI of all study participants were described using means and standard deviations. A univariate analysis using one-way ANOVA was applied to test the differences in means between continuous variables (BMI, height, weight, waist circumference, hip circumference, and mothers' menarcheal age) and the three categorized menarcheal age groups, followed by Tukey's test for pair wise comparison. Independent sample t-test was used to determine the menarcheal age difference between private and governmental students and between Saudis and non-Saudis. Chi-square test was used to test the

associations between age at menarche categories and other discrete variables (BMI categories, demographics, dietary variables and physical activity factors) and to compare the differences in socio-economic characteristics between private and governmental schools. Karl Pearson correlation coefficients were calculated to determine the relation between menarcheal ages of mothers and daughters, and the relation between BMI, and all other anthropometric variables with age at menarche. The results were considered statistically significant with a P value of <0.05.

ETHICAL CONSIDERATIONS

The study has been approved by the Fast Tract Ethical Review Board of Research in King Khalid University Hospital in Riyadh, KSA. Both mothers and daughters were invited to participate voluntarily. The daughters were all below the legal age, thus the informed consent was signed by their mothers. The consent form indicated the purpose of the study and the right of the participant to withdraw at any time without any obligation towards the study team. Participant's anonymity was assured by assigning each of them with a code number for the purpose of analysis only. No incentives were given to the participants. All measurements were obtained in accordance with the ethical standards laid down in the consent form. Approval for taking these measurements was included within the consent form.

RESULTS

A total of 324 out of 364 students had responded to our study, constituting a response rate of 89.01%. Out of the 324, 20 (6.2%) students were excluded, of which 9 returned incomplete questionnaires and 11 reported diagnosed conditions of (4 students) thyroid disease, (2 students) musculoskeletal disorders, (1 student) epileptic, (1 student) leukemia, and (3 students) reported taking long-term hormone replacement treatments or corticosteroids. The remaining total of students were 304, in which the number of students from governmental schools were 171 (56.25%), whereas, the number of students from the private school were 133 (43.75%). The mean age (SD) of students was estimated at 12.52 (2.08), 165 (54.3%) of whom attained menarche and 139 (45.7%) still haven't reached their menarcheal age. The number of Saudi students 166 (54.6%) was slightly higher than non-Saudi students 138 (45.4%). There were 80 (26.3%) subjects whose monthly family income is > 25000 SR. About 130 (42.8%) study subject's father education was bachelor degree. [Table 1]

Table 1: Distribution of demographic and socio-economic characteristics among female students (n=304) of ages 9-16 years

Characteristic	Frequency	%
Menstrual status		
Menses	165	54.3
Non-menses	139	45.7
Nationality		
Saudi	166	54.6
Non-Saudi	138	45.4
School		
Private	133	43.75
Governmental	171	56.25
Family monthly income (Saudi Riyals)		
<5000	80	26.3
5000-14,999	92	30.3
15,000-25,000	52	17.1
>25,000	80	26.3
Household characteristics		
Apartment	131	43.1
Small villa	86	28.3
Big villa	87	28.6
Father's education		
<High school	77	25.3
Diploma	72	23.7
Bachelors	130	42.8
Ph.D.	25	8.2
Mother's education		
<High school	94	30.9
Diploma	79	26.0
Bachelors	114	37.5
Ph.D.	17	5.6
Family members		
<4	38	12.5
5-7	192	63.2
8-10	66	21.7
>11	8	2.6

The mean BMI (Standard deviation (SD)) among all study participants, both menstruating and non-menstruating, was 21.38 (4.22). The median BMI was 21.0766 (maximum: 35.5, minimum: 13.79). The prevalence of obesity and overweight was 4.9% and 10.2%, respectively. The majority (79.9%) had BMI within the normal range, and 4.9% students were underweight. Among the menarcheal group (n=165), the mean age at menarche (SD) was estimated at 12.08 (1.28). Median age at menarche was 12 (range: 8-15) of whom 42 students (25.3%) attained menarche at less than 12 years of age. The majority 106 (63.9%) attained it between 12 to 13 years of age, and 17 students (10.2%) reached menarche above 13 years of age.

There was no significant difference between mean age at menarche (SD) in Saudis and non-Saudis, 11.96 (1.47) and 12.20 (1.04), respectively (p=0.227). The difference between the mean menarcheal age in private school students (11.59 years) and governmental school students (12.34 years) was statistically significant (p<0.001). When comparing the socioeconomic determinants between private and governmental school students, we found that private school students generally come from a higher socioeconomic status than governmental school students

and the difference in all socioeconomic determinants between both populations was statistically significant (P < 0.001). [Table 2] The mean age at menarche didn't vary significantly among the different BMI categories. [Table 3]

Table 2: Distribution and comparison of socio-economic characteristics between private and governmental school students (n=304), ages 9-16 in Riyadh, Saudi Arabia, 2013

Characteristics	Private (n=133) (%)	Governmental (n=171) (%)	P-value
Family's monthly income			
<5000	5 (3.8)	75 (43.9)	<0.001*
5000-14,999	19 (14.3)	73 (42.7)	
15,000-25,000	39 (29.3)	13 (7.6)	
>25,000	70 (52.6)	10 (5.8)	
Household characteristics			
Apartment	22 (16.5)	109 (63.7)	<0.001*
Small villa	46 (34.6)	40 (23.4)	
Big villa	65 (48.9)	22 (12.9)	
Mother's education			
<High school	3 (2.3)	91 (53.2)	<0.001*
Diploma	25 (18.8)	54 (31.6)	
Bachelors	90 (67.7)	24 (14)	
Ph.D.	15 (11.3)	2 (1.2)	
Father's education			
<High school	1 (0.8)	76 (44.4)	<0.001*
Diploma	17 (12.9)	55 (32.2)	
Bachelors	94 (70.7)	36 (21.1)	
Ph.D.	21 (15.6)	4 (2.3)	
Number of family members			
<4	24 (18.0)	14 (8.2)	<0.001*
5-7	93 (69.6)	99 (57.9)	
8-10	15 (11.3)	51 (29.8)	
>11	1 (0.8)	7 (4.1)	

*Using Chi-square test, statistically significant differences p<0.05

Table 3: Comparison of mean age at menarche of menstruating female students of ages 9-16 years in relation to study variables (nationality, type of school, BMI and age groups)

Characteristic	Mean age at menarche (SD)*	P-value
Nationality		
Saudi	11.96 (1.47)	0.227
Non-Saudi	12.20 (1.04)	
School		
Private	11.59 (1.30)	<0.001+
Governmental	12.34 (1.19)	
Body mass index		
Underweight	11.5 (0.7)	0.715
Normal	12.06 (1.37)	
Overweight	12.08 (0.92)	
Obese	12.45 (0.82)	
Age groups		
Less than 12	10.42 (1.13)	<0.001+
12-14	11.96 (1.07)	
Above 14	12.41 (1.4)	

*Standard deviation, +Statistically significant (P<0.05)

The mean (SD) height in menstruating students was 155.95 (6.62) cm, the mean weight (SD) was 55.72 (11.54) kilograms, the mean waist and hip circumference5 were 73.45 (8.86) cm and 94.88 (10.25) cm. Age at menarche was found to be positively correlated with height (r=0.205, P=0.008). However, it didn't show any significant correlation with BMI or any of the other anthropometric measures (weight, waist and hip circumference) (P>0.05). The mothers mean menarcheal age (SD) was found to be 13.13 (1.67) years. Their median age at menarche was 13 (range: 9-19 years). There was a positive correlation between the menarcheal ages of the menstruating students and their mothers (r =0.411, P<0.001). [Table 4]

The prevalence of obesity and overweight defined as BMI-for-age among the three named menarcheal age categories were 16.7%, 22.7% and 23.5%. No significant association was observed between the defined BMI categories and the three categorized menarcheal ages groups (P=0.85). [Table 5]

Factors influencing BMI and general lifestyle, including consumption of fast food and fruits and vegetables per week, hours of television watched, physical activity levels, and sporting activity times per week indicates no association with menarcheal age (P>0.05).

DISCUSSION

The importance of age at onset of menarche in relation to women's future overall health is a topic that has been scarcely discussed in oil-rich countries, such as Saudi Arabia, due to the conservative nature of the culture. The estimated mean age at menarche in this study, among menarcheal students ages (9-16) years old, was found to be 12.08 years. The calculated age at menarche was less than previously reported in Riyadh. It was almost a year less compared to the estimated mean of 13.05 years of age observed in Saudi women, in the report published in 2004, and 1.14 years less than the age at menarche dated 3 decades ago, both of which were calculated in Riyadh, Saudi Arabia.[15] A study on age at menarche and reproductive history in Saudi Arabia was investigated using data from a cancer survey conducted in Riyadh in 1986 among 2,675 women aged 14-59. The results showed a decline in mean age at menarche by 0.4 years in women born during the past 20 years, as compared with women born 45 years ago.[15] The downward trend of the menarcheal age was also noted in other regions of Saudi. A mean mearcheal age of 15.1 years was established for young Saudi girls in Western Saudi Arabia of Jeddah, whereas 13.07 and 13.81 years for girls from small and large families residing in the Asir Region, Southern Saudi

Table 4: Comparison of the students' mean anthropometric measurements, and their mothers' menarcheal age with their age at menarche and their correlation (pearson correlation)

Study variables	Less than 12		Age at menarche (12-13)		More than 13		P*	'r'**
	Mean	SD#	Mean	SD#	Mean	SD#		
Anthropometric measurements								
BMI	22.88	3.42	22.84	4.27	22.23	3.85	0.836	−0.033
Height (cm)	154.17	6.69	156.28	6.67	158.32	5.30	0.064	0.205++
Weight (kgs)	54.72	10.64	55.96	11.89	56.05	12.00	0.835	0.056
Waist (cm)	71.88	6.98	73.58	9.44	76.53	8.88	0.184	0.121
Hip (cm)	93.97	10.03	94.98	10.60	96.62	8.74	0.663	0.105
Mother's age at menarche	12.21	1.55	13.10	1.65	14.11	1.32	<0.001+	0.411++

*P-values from analysis of variance (ANOVA test). +P-value<0.05 is considered statistically significant. ++Statistically significant correlations (P<0.05). #Standard deviation. **Correlation coefficient

Table 5: Frequencies and percentages of age at menarche among BMI categories in menarcheal school students, ages 9-16 years, in Riyadh, Saudi Arabia 2013

Age at menarche (years)	Underweight (%)	Normal (%)	Overweight (%)	Obese (%)	Total
Less than 12	1 (2.4)	34 (80.9)	6 (14.3)	1 (2.4)	42
Between 12-13	1 (0.9)	81 (76.4)	15 (14.2)	9 (8.5)	106
Above 13	0	13 (76.5)	3 (17.6)	1 (5.9)	17
Total	2 (1.2)	128 (77.6)	24 (14.5)	11 (6.7)	165

Arabia. Another study conducted on age at menarche among adolescents in a gulf country, found the mean age at menarche to be 12.41 in Kuwait, 2013.[16] Similar findings were confirmed in Middle Eastern countries; In Egypt 1365 Egyptian girls attending eight different schools in the Cairo region and representing three strikingly different socio-economic sectors, the mean ages at menarche were estimated at 12.59 (0.29) for the high-class girls in Cairo; 13.09 (0.17) for the middle-class girls in Cairo; 13.89 (0.18) for rural agricultural areas.[17] Jordan expressed the mean age at menarche as 13.79 (1.23).[18] Iran reported an average age at menarche of 12.5 (1.1) years.[19] Turkey also described the mean age at menarche, in 2002, as declining from 13.6 (1.39) to 12.82 (1.07).[20] These findings collectively suggest a downward trend in age at menarche onset over time similar to that in western countries. Additional studies have also confirmed that menarche occurs earlier than it once did in many socioeconomically varied parts of the world, especially in Europe and North America.[21,22] Japan, UK, Croatia, Ireland, Italy also described menarcheal ages indicating a worldwide trend of lower ages.[23-27] Among the lower-income countries, Ethiopia (16.9 years), Nigeria (15.26 years), India (13.22 years), and Argentina (12.84) established the same declining trend.[28-31]

Concurrent improvements in living standards, hygiene, nutrition, and healthcare, amplified by the profound impact of oil-provoked modernization among Gulf countries, are considered to result in earlier sexual maturation.[15] This suggests that the increased prevalence of childhood overweight could lead to an earlier age of menarche.[26] Many studies focused on secular increases in childhood obesity and their relevance for secular changes in the timing of puberty.[32] Data from national surveys of US children, showed that the prevalence of overweight increased dramatically from 1976-1980's to 1999-2004.[33,34] The study demonstrated the downward secular trend in mean menarcheal age in the US during the same period, which suggested a parallel between an increase in the prevalence of overweight and a secular trend toward earlier timing of puberty. Driven by the previous rationale, body mass index trends in Saudi Arabia were examined and revealed a rising trend in BMI among Saudi adolescents, verifying that Saudi Arabia followed the world in the increasing secular trend in obesity, which is particularly relevant, as it suggests the decline in secular trends of age at menarche, at the same time as obesity has risen as a global epidemic.[35] One of the possible explanation, is that higher levels of pre-pubertal BMI could be a cause of early menarche, by increasing the production of estrogen through various mechanisms. Another rationalization suggests that early menarche associated with higher levels of estrogen increases fat deposition in peripheral adipose tissues.[36] Higher BMI was an effect caused by early menarche, rather than a cause. Thus, cross-sectional studies do not allow the verification of the temporal sequence of events surrounding age at menarche. A number of cross-sectional and longitudinal studies substantiated the inverse relationship between BMI and age at menarche, and affirmed it as a key player to menstrual onset.[15,36,37]

Other studies indicated the critical weight hypothesis; they showed that weight influenced by a certain level of leptin, a protein hormone that regulates body weight, metabolism

and reproductive function, is necessary to trigger the reproductive ability of young women. Therefore, it is likely that fat cells exert their regulatory effect on menarche through synthesis of leptin.[38] A critical blood leptin level is necessary to trigger reproductive ability in women, suggesting a threshold effect, or at least a body composition of 22% fat to trigger menstrual cycling in women.[9] Studies hypothesized that body fat distribution, despite low levels of total body fat, is of relevance to the onset of menarche.[38] This demonstrated no significant correlation with either waist or hip circumferences.

The current study found no correlation between menarcheal age and BMI or with weight, waist and hip circumferences, which could be attributed to the small acquired sample size of menarcheal students. In addition, some of the measurements were obtained considerably beyond the onset of age at menarche; another limiting factor for the chosen cross-sectional study design. However, the results of our study expressed a significant positive relationship which supports the general belief that girls who attain menarche at a later age will eventually grow taller, compared to girls who attain menarche at an earlier age. One explanation to this relation is the earlier closure of the epiphyseal growth plates in menstruating girls, due to the increase in ovarian estrogens in girls reaching menarche at an earlier age. Thus, a delay in menarche would allow more growth of the long bones before the epiphyses unite and would result in an increased adult height, denoting that our finding was a manifestation of age at menarche rather than a predictor, especially considering the fact that all anthropometric measurements for the menarcheal students in this study were obtained post-menarche.[3]

The difference between the menarcheal ages in private school students and government sponsored school students was attributable to the different socioeconomic statuses noted between the schools' attendees. This negative correlation is supported by Marshall and Tanner's study, which inferred that children of poor socio-economic portion take about a year more to mature than their counterparts in the upper socioeconomic portion.[37] Furthermore, higher parental education has been associated with earlier timing of puberty.[10] We found that students belonging to the higher socioeconomic classes had smaller families and lower ages at onset of menstruation, supporting a study conducted in Jeddah, Saudi Arabia, with similarities in culture and socioeconomic ranking. It stated that the number of siblings is a rough indicator of the family's socio-economic level, and that menarcheal girls belonging to smaller families had their menarche earlier than those belonging to family members more than four.[10] The reasoning behind this correlation remains unknown and is yet to be determined. However, it is safe to assume that the socioeconomic burden even at the level of family members can have an effect on growth, which could even stall puberty and therefore menarche.

Our study has revealed a significant correlation between the students' menarcheal ages and that of their mothers. Although the validity of age at menarche self-reported in adulthood has shown different levels of reliability, this study overcame the possible recall bias through specified questions in the provided survey. The positive correlation between the menarcheal ages of the menstruating students and their mothers serve as additional proof to the possible genetics role in age at menarche, as demonstrated by several studies.[1] Although the specific genetic determinants are unknown, evidence for hereditary influences on the age at menarche is derived from studies that show a trend for maternal age at menarche to predict daughter's age at menarche, a finding that persisted despite variations in environmental influences such as the socioeconomic status, nutritional state and physical activity of the girl.[7]

LIMITATIONS

The cross-sectional design does not enable us to determine the temporal sequence of events surrounding age at menarche. Also, the small sample size, wide age range, and the large number of those who have not yet attained menarche but were included to avoid selection bias, does not allow significant comparisons among menarcheal groups. Selection bias was overcome by systematic sampling adopted within the schools. However, as with all epidemiologic studies that use self-reported information, the potential for exposure misclassification should be accounted. Despite these limitations, this study successfully accomplished its primary methodological aim in providing preliminary data for the need of prospective longitudinal studies of menarche.

CONCLUSION

In conclusion, the mean age at menarche among present-day students in Riyadh was 12.08 years. There is an observed trend in the decline of age at onset of menstruation within the region and is considered a determined fact globally. When looking at the body mass index as a possible cause for early onset of menarche, our data showed no such correlation. However, our study found a notable difference in menarcheal age, between governmental and private school attendees, thus highlighting the role of socioeconomic status. A positive correlation was found between the mothers mean menarcheal age and their daughters, indicating that the mothers' age at menarche can be a good predictor for their daughters' onset at

menstruation. This study aimed to investigate these determinants locally, however restricted it may be, it remains a step forward in determining any causes for this change, and will encourage others in the medical field to adopt an interest in this issue.

RECOMMENDATIONS

Regional longitudinal studies should be conducted in order to monitor changes in age at menarche. This is important in our setting, due to the high reported prevalence of breast cancer. In view of these potential consequences in later life, modifiable factors influencing timing of menarche should be of public health interest in Saudi Arabia. Although this study did not determine a negative correlation between BMI and age at menarche, obesity rates in childhood and its effects on sexual maturation should still be examined within the region. Also, documentation of the age at menarche should be adopted in schools and healthcare facilities with annual anthropometric measurements. Lastly, it is required to determine a standard for the average normal menarcheal age amongst Saudis to be used as a reference for physicians, instead of referring to Western values.

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Authors Contribution:
SAS - Analysis of the data and revision of the manuscript; **RTH -** Concept and design of the study, literature review, data collection, statistical analysis and interpretation, preparation of the first draft of the manuscript and critical revision of the manuscript; **SFA -** Concept and design of the study, literature review, data collection, statistical analysis and interpretation, preparation of the first draft of the manuscript and critical revision of the manuscript; **GMA -** Concept and design of the study, literature review, data collection, statistical analysis and interpretation, preparation of the first draft of the manuscript and critical revision of the manuscript; **HFA -** Concept and design of the study, literature review, data collection, statistical analysis and interpretation, preparation of the first draft of the manuscript and critical revision of the manuscript; **LMA -** Concept and design of the study, literature review, data collection, statistical analysis and interpretation, preparation of the first draft of the manuscript and critical revision of the manuscript; **SSF -** Concept and design of the study, literature review, data collection, statistical analysis and interpretation, preparation of the first draft of the manuscript and critical revision of the manuscript; **MFN -** Concept and design of the study and critical revision of the manuscript.

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