Original article

Prevalence and Predictors of Insulin Resistance in Overweight and Obese Children and Adolescents: A Hospital-based Study

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Abstract. *Background/Aim:* To estimate the prevalence and predictors of insulin resistance (IR) among overweight and obese children and adolescents. *Material and Methods:* Data of this cross-sectional study included 62 overweight and obese children and adolescents (8-19 years of age), who visited the pediatric endocrinology clinic of King Abdulaziz University Hospital, Jeddah, Saudi Arabia. Participants' sociodemographic and health characteristics, dietary habits, physical activity, anthropometric measurements, and values of homeostasis model assessment of insulin resistance (HOMA-IR) were evaluated. Multiple regression analyses were conducted with [95% confidence intervals].*Results:* Among our sample, 59.7% of the participants (n=37) were insulin resistant. Among the evaluated predictors, physical activity and waist circumference (WC) predicted the risk for IR (B=-0.218 [-0.410 to -0.26] and B=0.127 [0.001, 0.016], respectively). Examining the associations between HOMA-IR values and anthropometric measurements while stratifying by maternal educational status revealed that the associations between WC and waist-hip ratio with IR were mediated by maternal educational status, and those associations were only observed in children of less educated mothers (B=0.014 [0.004, 0.024] and B=2.156 [0.635, 3.676], respectively).*Conclusion:* High prevalence of IR was observed among our sample. Future studies are needed to investigate the nationwide prevalence and predictors of IR among overweight and obese children and adolescents. Special attention should be paid to children of low-educated mothers for early detection and management.

Key words: insulin resistance, body mass index, children, adolescents, overweight, obesity

Introduction

Childhood obesity is a significantly rising public health concern that has reached epidemic proportions globally (1). The number of obese children has increased greater than ten-fold in the recent decades (2). In Saudi Arabia, the rapid economic and nutritional transitions have led to greater obesity trends over the past years (3). The existing data indicate that the prevalence rate of obesity among children and adolescents in Saudi Arabia has risen from 9.3% in 2004 to 18.2% in 2016 (4).

Childhood obesity is associated with an increased risk for several metabolic disorders, including insulin resistance (IR) and type-2 diabetes mellitus (T2DM) (5, 6). In particular, IR is the most common metabolic alteration related to obesity and is considered as a key element for the development of T2DM (7). Altered fat partitioning between subcutaneous and visceral adiposity tissues or ectopic sites has been linked to the risk of obesity-related IR in childhood (7). Despite the association of total adiposity with IR, excess abdominal adiposity in children and adolescents has been associated with greater risk for IR (7).

IR in children and adolescents has been also associated with the development of T2DM. In the recent years, rising rates of T2DM among children in the Arab countries have been observed (2). A study conducted in Saudi Arabia in 2012 has estimated the prevalence of T2DM among children as 9.0% (3). However, a major concern in Saudi Arabia is the high prevalence of undiagnosed T2DM among children. In 2015, over 90% of children and adolescents with diabetes were found unaware of their disease (4). Considering that the condition of IR is a possible reversible state with the proper management, special emphases should be placed on early detection and management to prevent, or delay, the development of T2DM later in life (8). A key step might involve screening overweight and obese children and adolescents for IR, as obesity has been widely recognized as a significant predictor for the risk of IR (9).

Several factors are believed to be involved in the pathogenesis of obesity-related IR, such as genetics, puberty, and sedentary lifestyle. Lifestyle behaviors of children can be largely influenced by maternal role in modulating the environment (10). Studies have shown that maternal adherence to healthy lifestyle practices is associated with lower risk of obesity in children (10). Other studies suggested that children of mothers with lower education levels have higher odds of being obese compared to those of higher educated mothers (11). Yet, it remains unclear whether maternal educational status influences the association between children's weight status and the risk of IR and further investigations are needed.

Despite the fact that the rates of obesity and T2DM are increasing globally and among the population of Saudi Arabia across all ages (4, 12), recent data regarding the prevalence of IR among overweight and obese children are lacking. This study aimed to investigate the prevalence and predictors of IR among overweight and obese children and adolescents. In this context, we also investigated whether the associations of the adiposity indices with IR are mediated by maternal education.

Materials and Methods

Study sample

To estimate the prevalence of IR among children and adolescents, we intended to include data of at least 61 participants, with a total width of confidence interval=0.20, expected proportion of children with IR estimated as 20%, and 95% confidence level (13). The participants were recruited from the pediatric endocrinology clinic of King Abdulaziz University Hospital, Jeddah, Saudi Arabia. The eligibility criterion included overweight and obese children and adolescents aged between 8 and 19 years. The exclusion criteria included participants diagnosed with DM or other endocrinopathies or liver disease, participants who are taking steroid medications, and those with BMI-for -age z-score (BMIz) ≤+1. The participants with their parents were informed about the study objectives and protocol, and parents were invited to sign the informed consent. The final analyses of this cross-sectional study included data of 62 participants.

A questionnaire was utilized to collect data related to sociodemographic characteristics and medical history, dietary habits, and physical activity. The questionnaire items were translated into Arabic using the forward-backward method and pilot tested on a small sample (excluded from the analyses) to ensure the clarity of the translated items and that the original meanings of the items are retained (14). Data were collected by three trained research assistants (dietetic professionals). The research assistants read each question and its corresponding options aloud, and answers of the participants were recorded accordingly. The study was conducted according to the rules of the Declaration of Helsinki and was ethically approved by the Unit of Biomedical Ethics, King Abdulaziz University Hospital (Reference No. 184-16). Confidentiality was maintained for all participants.

Sociodemographic characteristics and medical history

Parents of children reported information regarding their child's gender, Saudi nationality, maternal education, and family history of T2DM and obesity. Participants' age was calculated based on their date of birth. The pubertal stage was self-rated using the Tanner scale (15, 16).

Dietary habits and physical activity

Dietary habits and habitual physical activity were assessed using questions adapted from previously validated questionnaires (17, 18). The participants were asked about the frequency of consuming a serving of fruits, vegetables, milk and dairy products, desserts, soft drinks, and fast foods. The response options for each item were "never," "less than once a week," "once a week," "2-4 days/week," "5-6 days a week," "once a day, every day," and "every day, more than once" (17). The participants were guided throughout the questions on how to correctly define the serving size of each item.

A definition of physical activity was explained to the participants as "any activity that usually increases your heart rate and makes you get out of breath some of the time," with examples of qualifying activities followed by asking the following question: "In a typical week, do you participate in 60 minutes or more of moderate-to-vigorous physical activity every day?" Response options were recorded as "no" or "yes" (18).

Anthropometric measurements

Weight (in kg) and height (in cm) of the participants were measured using a digital scale with a height rod (Detecto Solo, USA). Waist and hip circumferences (in cm) were assessed following the World Health Organization (WHO) measurement protocol (19), and the waist-to-hip ratios (WHRs) and waist-to-height ratios (WHtRs) were calculated. The body fat percentage (BF%) was estimated using a digital bioimpedance analyzer (OMRON BF511, Japan) while participants were barefoot and wearing light clothes. Using the gender-specific BMI-for-age of the 2007 WHO growth chart as a reference, participants were classified as overweight or obese if their BMIz was >+1 or >+2 standard deviations (SD), respectively (20).

Biochemical data

Laboratory data of fasting insulin and fasting plasma glucose (FPG) were collected from the medical records of the participants within one week of the anthropometric assessment. Values of the homeostasis model assessment of insulin resistance (HOMA-IR) were calculated by multiplying fasting serum insulin (μU/mL) and FPG (mmol/L) divided by 22. As recommended by Cuartero et al., the cutoff value of 3.43 was selected in the present study to identify participants with IR, as it has been validated across children at different pubertal stages (21).

Statistical analysis

Descriptive statistics were calculated for sociodemographic and health characteristics. Mann-Whitney, Kruskal-Wallis, and Spearman's correlation tests were used to test the univariate associations of studied variables with HOMA-IR, and two-sided tests at a significance level less than 0.05 were considered. Multivariate linear regression analyses and associated [95% confidence intervals] adjusted for child's age, gender, and puberty stage were conducted to model the associations between HOMA-IR values and the potential predictors, including sociodemographic and health characteristics, dietary habits, physical activity, and anthropometric measurements. Residuals of HOMA-IR were not normally distributed; therefore, a log-transformed variable was used. Additional regression analyses were performed to investigate whether the associations between the anthropometric measurements and IR were modified by maternal educational status. Data analyses were performed using the IBM SPSS Statistics for Mac, version 24.0 (IBM Corp., Armonk, N.Y., USA).

Results

Sample characteristics and associations with HOMA-IR

Table 1 summarizes the participants' sociodemographic and health characteristics, dietary habits, physical activity, anthropometrics, and laboratory values. The medians and interquartile ranges of fasting insulin levels, FPG levels, and HOMA-IR values were 17.1 (13.1, 30.9) μIU/mL, 91.8 (88.2, 99.5) mg/dL, and 3.75 (2.93, 7.14), respectively.

Responses to the physical activity question indicated that approximately half of the participants

Table 1. Characteristics of the participants and the associations with HOMA-IR

Variable		**n= 62**	***P*-value***
Gender, n (%)	Male	29 (46.8)	0.944
	Female	33(53.2)	
Age, mean (SD)		12.6 (3.04)	0.563
Saudi	Yes	39 (62.9)	0.157
	No	23 (37.1)	
Maternal education, n (%)	Less than college degree	34 (54.8)	0.493
	college degree or greater	28 (45.2)	
Family history of obesity, n (%)	No	22 (35.5)	0.866
	Yes	40 (64.5)	
Family history of T2DM, n (%)	No	23 (37.1)	0.716
	Yes	39 (62.9)	
Family history of hypertension, n (%)	No	25 (40.3)	0.651
	Yes	37 (59.7)	
Puberty stage, n (%)	One	10 (16.1)	0.197
	Two	18 (29.0)	
	Three	18 (29.0)	
	Four	13 (21.0)	
	Five	3 (4.80)	
Daily physical activity for ≥ 60 minutes, n (%)	No	33 (53.2)	0.013
	Yes	29 (46.8)	
Weight in kg, mean (SD)		67.2 (18.2)	0.001
Height in cm, mean (SD)		147.2 (12.8)	0.001
Insulin µU/mL, mean (SD)		33.7 (49.8)	
FPG mg/dL, mean (SD)		92.3 (10.4)	
HOMA, mean (SD)		7.72 (12.0)	

* Mann-Whitney and Kruskal-Wallis tests were used for categorical variables and Spearman rho test was used for continuous variables. HOMA-IR, homeostasis model assessment of insulin resistance; T2DM, type-2 diabetes; BMIz, body-mass-index z-score; FPG, fasting plasma glucose; SD, standard deviation.

did not typically participate in daily physical activity (53.2%, n=33). Additionally, a large proportion of the participants reported consumption of fruits and vegetables less than once a day (75.8%, n=47 and 51.6%, n=32, respectively). Consumption of sweets and diary for more than once a day was reported by approximately one-quarter of the sample (n=15 and n=16, respectively), while the daily consumption of soft drinks and fast foods were reported by 17.8% (n=11) and 6.5% (n=4) of the participants, respectively (Figure 1).

HOMA-IR was not correlated with participants' age (r_s=0.08, *p*=0.563), or associated with the sociodemographic variables, family medical history, or dietary habits (*p*>0.050). However, the mean HOMA-IR value was found to be statistically significantly higher among the participants who did not typically participate in daily physical activity than that of participants reporting daily engagement in physical activity for ≥60 minutes (8.96±13.5 and 6.30±9.95, respectively, *p*=0.013). Furthermore, weight and height of the participants were positively correlated with HOMA-IR (r_s=0.40, *p*=0.001).

Table 2 illustrates the correlation between the anthropometric and biochemical indices. As expected,

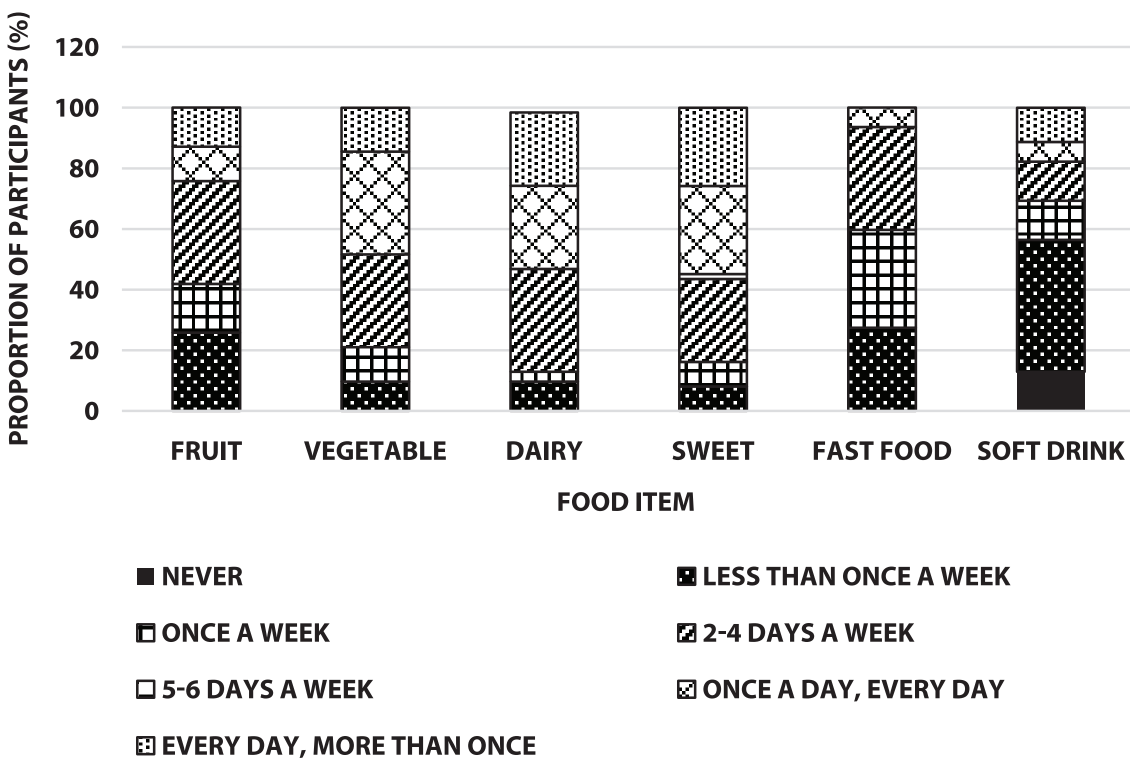

Figure 1. Participants' food intake (n=62)

Table 2. Spearman correlation matrix of the anthropometric and insulin resistance indices (n=62)

Correlation		BMIz	WC	WHR	WHtR	BF%
BMIz	r	1.00				
	p-value	--				
WC	r	0.468†	1.00			
	p-value	<0.001	--			
WHR	r	0.306*	0.540†	1.00		
	p-value	0.016	<0.001	--		
WHtR	r	0.717†	0.782†	0.633†	1.00	
	p-value	<0.001	<0.001	<0.001	--	
BF%	r	0.549†	0.426†	0.200	0.650†	1.00
	p-value	<0.001	0.001	0.118	<0.001	--
HOMA-IR	r	0.231	0.335†	0.237	0.151	0.228
	p-value	0.070	0.008	0.063	0.240	0.074
FPG (mg/dL)	r	-0.160	-0.129	-0.037	-0.064	-0.046
	p-value	0.214	0.317	0.776	0.620	0.723
Insulin (μU/mL)	r	0.277*	0.357†	0.244	0.169	0.257*
	p-value	0.029	0.004	0.056	0.188	0.044

* $p<0.05$, † $p<0.01$. HOMA-IR, homeostasis model assessment of insulin resistance; BMIz, body-mass-index z-score; WC, waist circumference; WHR, waist-to-hip ratio; WHtR, waist-to-height ratio; BF%, Body-fat percentage; FPG, fasting plasma glucose.

Table 3. Multivariate linear regression analyses* examining independent contributions of physical activity and anthropometric measurements to the variance of HOMA-IR†

Predictor	R^2	Beta coefficient	SE	P value	95% CI
Physical activity	0.134	-0.218	0.096	0.027	-0.410, -0.-26
BMIz	0.076	0.062	0.055	0.264	-0.048, 0.171
BF%	0.073	0.009	0.008	0.310	-0.008, 0.026
WC	0.127	0.008	0.004	0.034	0.001, 0.016
WHR	0.096	0.940	0.588	0.116	-0.238, 2.118
WHtR	0.073	0.619	0.600	0.307	-0.582, 1.820

*All models were adjusted for age, gender, and puberty stage and met the assumptions of multiple regression analysis; the variance inflation factors and tolerance test values of all variables included in the models ranged from 1.03 to 2.29 and 0.44 to 0.91, respectively. †HOMA-IR was log transformed. HOMA-IR, homeostasis model assessment of insulin resistance; BMIz, body-mass-index z-score; BF%, body-fat percentage; WC, waist circumference; WHR, waist-to-hip ratio; WHtR, waist-to-height ratio; SE, standard error; CI, confidence interval.

the anthropometric indices were statistically significantly correlated with each other (p<0.050). HOMA-IR was weakly positively correlated with the WC of the participants (r_s=0.34, p=0.008), whereas the insulin levels of the participants were found to be correlated with the BMIz (r_s=0.28, p=0.029), WC (r_s=0.36, p=0.004), and the BF% (r_s=0.26, p=0.044).

Prevalence and predictors of IR

Over half of the participants (59.7%, n=37) were diagnosed with IR, of whom 59.5% (n=22) were Saudis. Multivariate regression analyses did not indicate an association between IR and the sociodemographic and health characteristics or the child's dietary habits (p>0.050). The daily performance of physical activity accounted for 13.9% of the variance in HOMA-IR values, and statistically significantly predicted lower HOMA-IR values (B=-0.218 [-0.410, -0.-26], p=0.027), whereas WC predicted greater HOMA-IR values (B=0.127 [0.001, 0.016], p=0.034) and accounted for 13% of the variance in HOMA-IR values (see **Table 3**).

Adjusted associations between adiposity measurements and HOMA-IR stratified by maternal educational status

The associations of BMIz, BF%, and WHtR with HOMA-IR were not found to be statistically significant when stratified by maternal education (p>0.050) (Table 4). On the contrary, when the association between WC and HOMA-IR was stratified by maternal educational status, a significantly positive association was observed among participants whose mothers had less than a college degree, wherein the WC accounted for 36.9% of the variance in HOMA-IR values (B=0.014 [0.004, 0.024], p=0.008). Similarly, the stratified association between WHR and HOMA-IR by maternal education showed a positive association among children with lower maternal education levels, wherein the WHR accounted for 27.3% of the variance in HOMA-IR values (B=2.156 [0.635, 3.676], p=0.007).

Discussion

Considering the increasing rates of childhood obesity and T2DM in Saudi Arabia (4, 22), it became necessary to evaluate the prevalence of IR and identify its associated risk factors. The prevalence of IR among the overweight and obese children and adolescents in our sample was high (59.7%). Physical activity appeared to predict a lower risk of IR, whereas the larger WC predicted a greater risk of IR. Stratified associations between the anthropometric measurements and HOMA-IR by maternal educational status suggested a moderating effect on the associations between WC and WHR with IR in children of low-educated mothers.

The prevalence of IR among overweight and obese children have been investigated globally and lower proportions compared to our findings were reported. For

Table 4. Multivariate regression analyses* of HOMA-IR† to determine whether the associations with the anthropometric measurements according to maternal educational status were similar

Adiposity index Less than college degree		Maternal education	
		College degree or greater	
BMIz	R^2	0.238	0.295
	Beta	0.113	-0.100
	SE	0.083	0.083
	[95% CI]	[-0.057, 0.284]	[-0.181, 0.162]
	P value	0.183	0.907
WC	R^2	0.369	0.299
	Beta	0.014	-0.003
	SE	0.005	0.007
	[95% CI]	[0.004, 0.024]	[-0.017, 0.012]
	P value	0.008	0.707
BF%	R^2	0.230	0.309
	Beta	0.015	-0.008
	SE	0.012	0.012
	[95% CI]	[-0.010, 0.040]	[-0.033, 0.017]
	P value	0.223	0.506
WHR	R^2	0.375	0.298
	Beta	2.156	-0.285
	SE	0.742	0.795
	[95% CI]	[0.635, 3.676]	[-1.934, 1.365]
	P value	0.007	0.724
WHtR	R^2	0.273	0.344
	Beta	1.435	-1.224
	SE	0.790	0.946
	[95% CI]	[-0.184, 3.054]	[-3.186, 0.738]
	P value	0.080	0.209

* All models were adjusted for child's gender, age, physical activity, and puberty stage, and met the assumptions of multiple regression analysis; the variance inflation factor and tolerance test values of all variables in the models ranged from 1.08 to 2.98 and 0.34 to 0.87, respectively. † HOMA-IR was log transformed. HOMA-IR, homeostasis model assessment of insulin resistance; BMIz, body-mass-index z-score; WC, waist circumference; BF%, body-fat percentage; WHR, waist-to-hip ratio; WHtR, waist-to-height ratio; SE, standard error; CI, confidence interval.

instance, a study conducted in Southern Italy evaluated the prevalence of IR among obese adolescents based on a national cutoff HOMA-IR level of >4.00 and reported a prevalence of 41.2% (23). In another study, a cutoff value similar to that followed in the present study was used among 220 obese adolescents residing in São Paulo. Approximately 33.2% of the participants were IR (24). However, in Saudi Arabia, data are limited. We were able to identify one study that evaluated the prevalence of fasting hyperinsulinemia among 57 obese Saudi children and adolescents in 2009 and reported a prevalence of 36.0% (25).

Saudi Arabia and several Arab countries have witnessed rapid economic development and changes to societal norms, and the sedentary lifestyle has become predominant (3). Based on the current recommendations, children are advised to "engage in at least one hour per day of moderate-to-vigorous physical activity" (26). However, a systematic review of physical inactivity prevalence among the Saudi population indicated that a large proportion of the community is physically inactive, with the prevalence among children and adolescents ranging from 25.7% to 86.1% across different studies (27). In the present study, physical inactivity was also reported in a large proportion of the sample (53.2%). Furthermore, the data indicated an inverse association between physical activity and the risk of IR. This finding is consistent with that of previous international longitudinal studies, where physical inactivity was found to be associated with IR independent of children's weight status (28). In Saudi Arabia, the existing evidence indicates that factors such as urbanization, extreme weather, and cultural perceptions are determinantal barriers to physical activity (27). Therefore, intensive efforts should be invested toward promoting physical activity among the Saudi society to control the increasing prevalence of obesity and the associated complications.

Among all the evaluated anthropometric measurements, only WC was found to be significantly associated with the risk of IR. Previous international investigations have been performed, but inconsistent findings were reported. For example, a cross-sectional study of healthy Korean adolescents reported significant associations between HOMA-IR and BMI, WC, WHtR, and WHR (29). Another study comprising Malaysian adolescents observed significant associations between HOMA-IR and BMI and WC, but BF% was not associated with HOMA-IR (30). However, a cohort study of 438 adolescents suggested that WC might better predict the risk of IR compared to BMIz, WHtR, or WHR (31). Despite the variations among the previous findings, the results of the present study support the hypothesis that the role of central obesity (apple shape) in predicting the risk of IR is possibly associated with the physiological and endocrine functions of the visceral fat tissue rather than the subcutaneous fat depots (pear shape) (32).

Our findings indicated that maternal education mediates the association between WC and WHR and IR. The association between maternal education and HOMA-IR values has been previously investigated, but conflicting results have been reported. For example, a study investigated the association between parental educational status and IR among Denmark, Estonian, and Portuguese children; a greater prevalence of IR among Denmark children of low educated parents was observed compared to those of parents with higher education levels. On the contrary, a positive association was observed among Estonian and Portuguese children (33). In the present study, we hypothesized that mothers with low educational levels in Saudi Arabia may have limited accessibility or knowledge about healthy food options, which could negatively affect the health status of their children. Additionally, maternal perceptions about the weight status of their children could further affect the feeding style and practices, wherein mothers of children perceived as underweight may provide high calorie foods with poor dietary quality. However, future studies are required to determine the role in which maternal education can be associated with IR in overweight and obese children. Qualitative studies investigating feeding practices employed among the population of different socioeconomic status could reveal behaviors specific to low-educated mothers that may exacerbate the risk of IR. Special attention should be paid to healthcare centers where children of low socioeconomic status are expected. It is important to highlight the need for nutrition intervention programs specifically tailored to parents with low educational status and their children to introduce possible strategies for weight management and to enhance children's nutritional status.

Limitations

Our findings might be generalizable only to overweight and obese children and adolescents in Saudi Arabia. Further, the results presented in this study do not infer causality due to the nature of the study design. Future longitudinal studies are needed to establish cause-and-effect relationships and to develop evidence-based interventions. Additionally, the assessment of puberty stage was self-rated. Yet, a recent cohort study validated the self-assessment method with serum testosterone and estradiol and suggested "fair" to "moderate" agreement (34). In fact, self-reported staging might be more feasible among this specific population due to people's perception of sexual and reproductive health related to religious and cultural beliefs (35). Moreover, previous studies have described the doubly labeled water method as the gold standard to assess physical activity (36). In the present study, assessment of habitual physical activity was based on a questionnaire item that has been previously validated among children and adolescents (18).

Conclusion

Findings of the present study have important clinical and public health implications that need to be considered. Given that IR was found to be highly prevalent among our sample, clinical practitioners may need to consider screening overweight and obese children for IR. However, future studies are needed to investigate the nationwide prevalence of IR among the overweight and obese children and adolescents. Our findings also provide additional evidence for the association of WC and physical activity with the risk of IR. Therefore, healthcare professionals need to monitor changes in WC of overweight and obese children and encourage them to adapt active lifestyle. Additionally, the associations between WC and WHR and IR in the present study were linked to maternal educational status. Therefore, special attention should be paid to children of less-educated mothers to enhance their knowledge and practices for weight reduction and risk management.

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