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Vitamin D Deficiency in Obese Children and its Relationship to the Components of the Metabolic Syndrome.

Hanan A. Alfawaz and Fadia Y. Abdel Megeid

Department of Food Science and Nutrition, King Saud University Riyadh, Saudi Arabia

Abstract: To examine the relationship between vitamin D status and components of metabolic syndrome such as body mass index (BMI), blood pressure (BP), fasting blood glucose (FBG),triglyceride (TAG), high density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C) in Saudi obese children. This is case- control study done among 120 obese children (cases) and 120 non- obese or normal weight children. The subject studied constituted 120 obese (≥95th percentile) comparing to normal weight child (120) representing different socio-economic districts who were attending the outpatient clinics at Hospital of Pediatric, King Saud Medical City, Riyadh City, Kingdom of Saudi Arabia (KSA). They were randomly selected. Their ages ranged between 9 and 14 year. This study was carried out from October to December 2012. Data were collected from the pediatric nutrition clinic (PNC) of the outpatient department (OPD); these children were referred to the nutrition clinic by the pediatricians for nutritional assessment and to be follow-up by dieticians for further nutritional assessment. Their main problems were obesity. A questionnaire was administered to the parents of all children. The questionnaire included socio-demographic data, the medical history comprised of medical illnesses such as hypertension in the subject Anthropometric and blood pressure were measured for all children. BMI was calculated for all children. Diagnostic criteria of MS was made based on the International Diabetes Federation's pediatric definition (IDF), namely waist circumference (WC) ≥ 90th percentile plus two or more of the following indices for all boys and girls: Triglycerides(TAG) ≥150 mg/dL (1.7 mmol/L), Blood pressure(BP) (Systolic ≥130 mmHg or Diastolic ≥85 mmHg), fasting blood glucose(FB) ≥100 mg/dL (5.6 mmol/L) and high-density lipoprotein cholesterol(HDL-C) ≤40 mg/dL(1.03 mmol/L). It was observed from our study that the frequency of MS was 17% in overweight/obese children It is important to note that obese girls had significantly higher frequency of MS (10%) than obese boys (7%). MS was not observed in non obese children. It was observed from our study that the obese children had significantly worse clinical profiles and higher anthropometric parameters (P<0.001) compared to non obese children. Also the obese girls children had significantly higher anthropometric and biochemical indices compared to obese boys P<0.001. Correlations of serum 25 hydroxyvitamin (OH) D (25(OH) D with metabolic variables, it is observed from our study that there negative correlation between the level of serum 25 (OH) and BMI, FBG, LDL-C and TAG as well as BP and there positive correlation between the level of serum 25(OH) D and HDL-C. (P< 0.01).

Key words: Obesity · Metabolic syndrome · Anthropometric parameters · Blood pressure · High-density lipoprotein cholesterol

INTRODUCTION

Vitamin D deficiency, as indicated by a serum concentration of 25 (OH) D level below 20 ng/ml (50 nmol/L) [1], is commonly present in obesity and has been implicated as a risk factor for MS [2]. With the increasing prevalence of overweight and obesity worldwide, especially in children and youth, the "pediatrics metabolic syndrome" has received increasing attention from a public health perspective [3]. MS is recognized as the clustering of risk factors of obesity, insulin resistance, dyslipidemia and hypertension associated with the subsequent development of (CVD) and diabetes mellitus type 2 (DMT2) [4]. In a recent population study, subjects with cardiovascular disease had a greater frequency of vitamin D deficiency than

Corresponding Author: Hanan A. Alfawaz, Department of Food Science and Nutrition, King Saud University Riyadh, Saudi Arabia.

those without [5]. In the KSA, several epidemiologic studies point to increased incidence of high risk factors for CVD. More than one-fourth of the Saudi adult population is hypertensive [6]; 40% of the same cohort has hypertriglyceridemia (≥1.69 mmol/L) [7] and 39% harbors the complete MS [8] Previous cross-sectional studies for adults have reported that low 25(OH)D concentrations are related to glucose intolerance, diabetes, insulin resistance, hypertension and MS[9]. Likewise, an association of serum 25(OH) D with insulin sensitivity and fasting glucose has been found in children [10]. Insulin resistance enhances the flux of free fatty acids to the liver and alters hepatic production of lipoproteins such as concentrations of TAG and small dense (LDL-C) are increased, whereas that of HDL-C is decreased [11]. With increased adiposity there is increased production of inflammatory markers which, in turn, promotes further exaggeration of insulin resistance. Studies done in Saudi children, on the other hand, reveal increased incidence of obesity due to improved nutrition [12] and obese children are usually sedentary and therefore less likely to play outdoors, their exposure to sunlight may be limited [6]. In addition, unhealthy high caloric food might be low in mineral and vitamin content [7, 8]. Both represent risk factors for developing vitamin D deficiency. Additionally, bioavailability of vitamin D in obese subjects might be low because of its deposition in a fat tissue [12] and higher body fat mass might be associated with a higher risk of vitamin D deficiency [13].

This study aims to assess the relationship between vitamin D status and components of MS, such as BMI, BP, FBG, TAG, HDL-C and LDL-C among obese children.

MATERIALS AND METHODS

This is a case-control study done among 120 obese children (cases) and 120 non-obese or normal weight children. The subject studied constituted 120 obese (≥95th percentile) child representing different socio-economic districts who were attending the outpatient clinics at Hospital of Pediatric, King Saud Medical City, Riyadh City, KSA. They were randomly selected. Their ages ranged between 9 and 14 year. This study was carried out from October to December 2012. Data were collected from (PNC) of the (OPD), these children were referred to the nutrition clinic by the pediatricians for nutritional assessment and to be follow-up by dieticians for further nutritional treatment. Their main problems were obesity. Exclusion criteria include subjects with any congenital abnormalities or cancer diseases (these patients suffered from vitamin D deficiency).

Tools of the Study: A questionnaire was administered to the parents of all children and was considered consent for their children's participation in the study. The interview was carried out by the researcher for approximately 20 minutes for each subject, in the outpatient diet clinic. At the beginning of the interview, the purpose was explained to the mother and assurance was given that all information will be treated with strict confidentiality and will be used for research purpose only. The patients/subjects medical record number was used to complete the medical history. The questionnaire included socio-demographic data, age, sex, parent's educational levels, occupation of the parents, medical history which was comprised of medical illnesses such as hypertension.

Anthropometric Measurements: Anthropometric measures comprised height, weight, midarm circumference, subscapular; triceps and skin fold thickness, WC, Hip circumference and Waist hip ratio (WHR). Height was measured to the nearest cm by stadiometer, obtained without shoes, back straight with buttocks and shoulders touching a wall and head forward. Weight was measured, to the nearest 0.5 Kg, by a spring balance. Calibration of the scale was made on a daily basis using two different standard weights. The child was weighed in light clothes (no shoes or heavy outer garments). BMI used as an indicator for obesity and was defined as weight over height squared: [wt in kg/ (ht in m) ^{2}], Obesity was defined as ≥95th percentile [14], under weight <5th percentile and over weight: BMI>85 percentiles. The midarm circumference was measured after measuring the left upper arm length was measured from the acromion to the olecranon with the metal tape. The child's forearm was raised to make 90^{o} angle during the measurement. The midpoint between the acromion and olecranon determined and marked on the dorsal surface of the arm. The triceps skinfold was measured between the acromion and olecranon and the subscapular skinfold was measured below the tip of inferior angle of scapula. The measurement was performed three times during the examination. Percentiles for the anthropometric measures as weight and height, Triceps and skinfold thickness [15] were obtained. The measurements of the present study

were related to age and sex and plotted on the percentile curves. WC was measured to the nearest cm at the level of umbilicus with the subject standing and breathing normally. Hip circumference was measured on the under wear at the most protruding part of the buttocks to the nearest cm. WHR was defined as the ratio of waist circumference to the hip circumference in centimeters [16].

Blood Pressure Examination: BP was measured for all children using random zero sphygmomanometer [17]. The child was seated at rest for at least 5 minutes before measurement. Two successive readings were taken approximately one minute apart. (National High Blood Pressure Education program, 1996)[18]. The children were considered hypertensive if they were on ≥95th percentile for both systolic and diastolic blood pressures.

Diagnostic Criteria: MS was diagnosed based on the IDF pediatric definition [19], namely waist circumference ≥90th percentile plus two or more of the following indices for all boys and girls:

- TAG ≥150 mg/dL (1.7 mmol/L).
- Bp (Systolic ≥130 mmHg or Diastolic ≥85 mmHg).
- FBG ≥100 mg/dL (5.6 mmol/L).
- HDL-C ≤40 mg/dL (1.03 mmol/L).

Biochemical Profile: Blood analysis for: 1) TAG and High HDL-C and LDL-C [20], FBG and Oral glucose Tolerance Test. Fasting plasma venous glucose =7.0 mmol/l (126 mg/dl) or 2) hour oral glucose tolerance test (OGTT) (with 75g with glucose) plasma venous glucose = 11.1 mmol/L (200mg/dl) [21]. Serum 25 (OH) D was measured by Roche Analyzer Cobas e601immunoassay [22].

Statistical Analysis: Data were expressed as mean ± S.E. and were analyzed statistically using SPSS version 12.0 software (SPSS, Chicago, III). The variables were compared using T-test and Chi- square test. Differences were considered statistically significant at P≤0.05. Pearson correlation and stepwise regression analysis were used to investigate the relationships between MS and anthropometric measurements [23].

RESULTS

Tables 1 describe the socio-demographic characteristic of the studied group. The mean age of the sample was 11± 2.1 years obese and10±1.7 in non obese children that ranges from 9 to 14. Most of the children's' fathers were Preparatory and Secondary education 40% and 41% obese and non obese children, respectively, 40% of fathers were employees in obese children compared to (50%) non obese children, most of the mothers received below essential education read and write (52%) obese children compared to (53%) in non obese children, The majority of mothers were house wives (70%) obese children compared to (68%) in non obese children. On describing the family income; most of the families of the studied group were sufficient and saving. There was no statistically significant difference between the two groups regarding to the education and occupation of the fathers and the mothers as well as the family income p>0.05. Diagnostic criteria of MS was made on the International Diabetes Federation's pediatric definition (IDF)[19], namely WC ≥ 90th percentile plus two or more of the following indices for all boys and girls: TAG ≥150 mg/dL (1.7 mmol/L), BP (Systolic ≥130 mmHg or Diastolic ≥85 mmHg), FB≥100 mg/dL (5.6 mmol/L) and HDL-C ≤40 mg/dL(1.03 mmol/L). Data presented in Table 2 indicated that the frequency of MS was 17% in overweight/obese children (according to IDF criteria patient must have three risk factors or more to be diagnosed as metabolic syndrome, the result show 4% and 3% from the boys had three and four risk factors, respectively and 5%, 5% from the girls had three and four risk factors, respectively). It is important to note that obese girls had significantly higher frequency of MS (10%) than obese boys (7%). MS was not observed in non obese children. Anthropometric and biochemical characteristics of the children are shown in Table 3 and Overweight/obese children had significantly worse clinical profiles and higher anthropometric parameters [height, weight, BMI, hip circumference (HC), (WHR), waist-to-height ratio, waist-to-hip ratio (WHR), TAG, HDL-C, LDL-C, SBP and DBP, p<0.001; p< 0.05] compared to non obese children. Comparison of anthropometric measurements, BP, biochemical characteristics of the studied groups regarding sex presented in Table 4 the obese girls children had significantly higher anthropometric and biochemical indices compared to obese boys (P<0.001). Correlations of serum 25(OH) D with metabolic variables it is observed from Table 5 that there negative correlation between the level of serum 25-hydroxyvitamin D and BMI,FBG, LDL-C and TAG as well as BP and there positive correlation between the level of serum 25(OH)D and HDL-C (P<0.01).

Table 1: Socio-demographic characteristics of the studied groups

	Obese No (120)		Non obese No (120)		
Description	No	%	No	%	P
Mean age (years)	11±2.1		10±1.7		
Range	9-14		9-14		
Gender					
Boys	55	46	55	46	>0.05
Girls	65	54	65	54	
Father`s education					
Read & write	40	33	38	32	>0.05
Preparatory, Secondary	48	40	49	41	
University	32	27	33	27	
Mother`s education					
Read & write	62	52	64	53	>0.05
Preparatory, Secondary	42	35	40	33	
University	16	13	16	14	
Father`s occupation					
Professional	47	39	46	38	>0.05
Employee	48	40	60	50	
Manual	25	21	14	12	
Mother's occupation					
Working	36	30	38	32	>0.05
House wife	84	70	82	68	
Family income					
Sufficient and saving	58	48	56	47	>0.05
Sufficient	54	45	55	46	
Insufficient	8	7	9	7	

Tablet 2: The metabolic risk factors in obese and non obese children

Body mass status	Obese (N0 120)				Non obese (No :120)			
	Boys		Girls		Boys		Girls	
Gender								
Risk factor	No	%	No	%	No	%	No	%
o/risk factor	19	16	18	15	54	45	60	50
+1/risk factor	16	13	19	16	1	1	5	4
+2/risk factor	12	10	16	13	0	0	0	0
+3/risk factor	5	4	6	5	0	0	0	0
+4/risk factor	3	3	6	5	0	0	0	0
Total	55	46	65	54	55	46	65	54

Table 3: Comparison of anthropometric measurements, blood pressure, biochemical characteristics of the studied groups

Parameters	Obese (120) (mean ±S.D)	Non obese (120) (mean ±S.D)
Anthropometric measurements		
Mid arm	21.4±5*	15.7 ±3
Triceps	12.9 ±4.1*	10±0.1
Sub scapular	11.8 ±6.4*	8.2 ±0.2
Waist circumference (cm)	77.4 ±7.1**	52.1±0.3
Hip circumference (cm)	90.9±8.8**	70.2 ±0.1
Waist height ratio	0.6 ±0.1**	0.4.1±0.1
Waist hip ratio	0.8 ±0.1**	0.7.4±2.1
Height(cm)	133.1±0.1**	125±0.2
Weight (kg)	47± 0.1**	26.5 ±0.1
BMI(kg/m^2)	26.9±0.1**	16.98±0.1

Table 3: Continue

Parameters	Obese (120) (mean ±S.D)	Non obese (120) (mean ±S.D)
Blood pressure		
Systolic BP	123.7 ±7.2 **	98.7 ±5.3
Diastolic BP	78.8 ±3.4 **	61.8 ±9.3
Biochemical characteristics		
FBG (mmol/L)	4. 1 ±1.9*	3.0 ±0.1
TAG (mmol/L)	1.8 ±0.1**	0.6 ±0.2
HDL-C (mmol/L)	0.9 ±0.1**	1.7 ±0.4
LDL-C(mmol/L))	4.7 ±2.4*	3.0±0.1
25(OH) D (nmol/L)	19.4±1.5**	26.4±3.6

**significance at P <0.001, * significance at p<0.05.

Table 4: Comparison of Anthropometric measurements, Blood pressure, Biochemical characteristics of the studied groups: sex

Parameters	Male (mean ±S.D)	Female (mean ±S.D)
Anthropometric measurements		
Mid arm	21.7 ±5	21.9±8
Triceps	13.4 ±7.1	13±8.2
Sub scapular	11.3 ±1.4	11.9 ±2.2
Waist circumference (cm)	76.3±0.3	77.1±0.0
Hip circumference (cm)	91.9±0.8	92.0 ±0.1
Waist height ratio	0.6 ±0.1	0.6±0.1
Waist hip ratio	0.8 ±0.1	0.8 ±0.2
Height(cm)	132.0 ±0.1	132.7±0.6
Weight(kg)	46.9±0.3	47.7±0.7
BMI(kg/m^2)	26.95±0.1*	27.4±0.1
Blood pressure		
Systolic BP	121.4±4.3*	127.6±2.3
Diastolic BP	79.5±2.2*	80.9±11.4
Biochemical characteristics		
FBG (mmol/L)	4.0.1 ±1.1	5.1±0.1
TAG (mmol/L)	0.8 ±0.1**	1.6±0.4
HDL-C (mmol/L)	1.8 ±2.4*	1.0±0.1
LDL-C(mmol/L)	3.0 ±0.3*	4.1±2.7
25(OH)D (nmol/L)	18±0.2 *	14±0.1*

**significance at p<0.001, * significance at p<0.05.

Table 5: Correlations of serum 25(OH) D with metabolic variables

Parameters	Correlation coefficients (r)	P value
BMI	-0.7 31	<0.01
FBG	-0.618	<0.01
TAG	-0.453	<0.01
HDL-C	0.443	<0.01
LDL-C	-0.434	<0.01
Systolic BP	-0.3 67	<0.01
diastolic BP	-0.3 12	<0.01

DISCUSSION

Vitamin D deficiency is commonly present in obesity and has been implicated as a risk factor for MS (2). The prevalence of children suffering from MS in our study was 17%, (according to IDF criteria patient must have three risk factors or more to be diagnosed as metabolic syndrome, the result show 4% and 3% from the boys had three and four risk factors, respectively and 5%, 5% from the girls had three and four risk factors, respectively). represented 10% of the girls and 7% of the boys and the obese girls children had significantly higher anthropometric and biochemical indices compared to obese boys, this is in agreement with those obtained by Ferreira *et al.* [24] who reported that the prevalence of the studied children in Brazil in 2007 suffering from MS was 17.3%, broken represented 10.7% of the boys and 25% of the girls. These figures are comparable with the results of another study that analyzed schoolchildren from a rural community in the USA and found figures of 10% for boys and18%for girls aged 7 to 18 years [25]. Also in agreement with our study are the results of the Bogalusa Heart Study which found that 17.2% of children aged 5 to 10 years exhibited three or more risk factors for CVD [26].

It was observed from the present study that overweight/obese children pose a higher risk for developing the MS with high significant ($p<0.05$) as

compared to normal-weight individuals. This agrees with the study by Wee *et al.* [27] who reported that 5.3% of overweight/obese children in metropolitan Kuala Lumpur had the MS with only 12% of the overweight/obese group being free from the MS risk factors. This is in sharp contrast to 83.9% of the normal-weight children who were free from all risk factors. The overweight/obese children pose a higher risk for developing the MS with O.R of 16.3 as compared to normal-weight individuals. A hospital-based study by Taha *et al.* [28] has reported that obese Saudi children and adolescents have multiple risk factors associated with MS. In Kuala Lumpur, another study reported that Ms was found in 1.3% of children aged 7 to 9 years [29]. It is observed from our result that significance lower level of serum 25(OH) D in obese children this is supported by Al-Daghri *et al.* [30], who reported that significant associations between serum 25(OH) D and cardio metabolic parameters support promising cardio protective benefits from vitamin D sufficiency at an early age. Follow-up with prospective clinical intervention studies are needed to validate this hypothesis. Regarding the correlation between serum 25(OH) D and metabolic parameters, it is observed from our result that there was negative correlation between BMI and the level of serum 25(OH) D. This is in agreement with those reported by Reinehr *et al.* [31], who examined obese children and found a significant increase in 25(OH)D levels after a lifestyle intervention induced weight loss. In a more recent study in adult women, weight loss was also associated with an increase of 25(OH) D levels and was accompanied by improved insulin resistance [32]. For treatment of vitamin D deficiency, it is important to note that the American Academy of Pediatrics (AAP) recommended that daily intake of vitamin D of 400 IU is insufficient to correct vitamin D deficiency in obese African American children [33]. New guidelines recommend much higher doses to treat vitamin D deficiency in children and adolescents, which is in particular important in obese subjects [34].

Also it is observed from our result that there was negative correlation between FBG and the level of serum 25(OH) D. This is in agreement with those reported by Ashraf *et al.* [35] who found a negative relationship between serum 25(OH)D and fasting glucose, which is in concordance with another pediatric study by Johnson *et al.* [36] which demonstrates an improvement in serum glucose after correction of vitamin D deficiency.Fasting glucose reflects endogenous hepatic glucose production and also reflects hepatic insulin resistance and the inability to regulate the hepatic glucose output is considered to be the key defect in type 2 diabetes. However, sites other than the liver may be involved in 25 (OH) D-mediated reductions in glucose. Chui *et al.* [37], in a study involving healthy, glucose-tolerant adults that controlled for sex, BMI, ethnicity and BP, reported a relationship of similar magnitude as ours between plasma 25(OH) D and fasting glucose concentrations.

As regards the correlation between serum 25(OH) D and lipid profile it is observed from our result that there was strong correlation between lower HDL-C and high LDL-C as well as TAG and the level of serum 25 (OH)D this agreement with study of Botella-Carretero *et al.* [38], in a cross-sectional study of 73 obese men and women, reported that vitamin D deficiency, defined as 25 (OH) D concentrations, 50 nmol/L, was associated with lower HDL-C and higher triglyceride TAG concentrations. They also reported a higher prevalence of vitamin D deficiency in obese individuals with MS than in those without. In the third National Health and Nutrition Examination Survey [39], adults in the lowest quartile of 25(OH)D had the greatest risk of elevated serum TAG ($\geq$150 mg/dl), suggesting a detrimental effect consequent to vitamin D deficiency. Similarly, in obese subjects 25(OH)D <50 nmol/l was associated with lower HDL-C and high TAG (38).This result was supported by Carr *et al.* [40], who reported that MS and obesity are associated with reduced HDL-C cholesterol concentrations, elevations of TAG, as well as increased concentrations of small dense LDL-C particles. Also, Vikram *et al.* [41] reported that the overweight and obesity in children and adolescent in Urban Asian Indian was significantly associated with dyslipidemia (hyper TAG and low levels of HDL-C). The association between low 25(OH)D levels and elevations in systolic and diastolic BP in our study confirms the observations of Burgaz *et al.* [42] in elderly men, in whom a higher prevalence of confirmed hypertension was observed among those with low concentrations of 25(OH)D. The active form of vitamin D 1, 25(OH) D is a potent endocrine suppressor of renin biosynthesis and a negative regulator of the renin-angiotensin system in humans [43].

CONCLUSION

Obese children exhibited a high prevalence of MS with more risk factors. In the light of these findings

intervention measures are necessary in order to prevent excessive weight gain during childhood. The 25 (OH) D concentrations in children and adolescents are inversely related to the plasma glucose concentration and positive association with lipid markers observed among the studied groups. A number of studies support an increase in daily vitamin D intake. The recent recommendation of the American Academy of Pediatrics to increase vitamin D intake to 400 IU/d (1 IU = 25 ng/d cholecalciferol) from 200 IU/d (44) is a step in that direction.

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