

## **Vitamin D supplementation influence on anthropometric indices, but not on blood pressure and lipid profile in women: a clinical trial study**

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**Running title:** Vitamin D Supplementation, Anthropometric indices, blood pressure and lipid profile.

**Abstract:**

**Introduction:** vitamin D deficiency has defined as a health problem in the worldwide. Recently, it has been shown that vitamin D deficiency may be related to insulin sensitivity, hypertension, hyperlipidemia, and obesity. These factors are linked to increased risks of serious health complications such as type 2 diabetes, CVD, stroke, and kidney failure. In this study, we aimed to perform an investigation about the effects of vitamin D supplementation on anthropometric indices, lipid profile, and blood pressure on obese and overweight women.

**Subject and method:** This double blind clinical trial was done on 53 overweight and obese women who divided into two groups which intervention group received vitamin D supplements with dozes 50000 IU/w for 6 weeks and another received placebo. The anthropometric indices, biochemical markers, and blood pressure measured before and after intervention, and independent-samples t- test and paired- samples t- test were used to compare the mean between and within group respectively.

**Results:** After using vitamin D supplementation for 6 weeks weight (wt), WC, Body Mass Index (BMI) were decreased significantly and serum vitamin D increased significantly compared to control group ( $p < 0/001$ ). Other factors including total cholesterol (TC), triglyceride (TG), low density lipoprotein cholesterol (LDLc), high density lipoprotein cholesterol (HDLc), and WHR did not change significantly ( $p > 0/05$ ).

**Discussion:** The evidence of this study suggests that supplementation of the vitamin D with dozes 50000 IU/w for 6 weeks in obese and overweight women lead to reduce in BMI, weight and WC significantly, whilst this study did not confirm the effect of vitamin D supplementation on lipid profile.

**Key words:** Vitamin D Supplementation, Anthropometric indices, Cholesterol, LDL- Cholesterol, HDL- Cholesterol, Triglyceride, Blood pressure.

**Introduction:**

Vitamin D deficiency is considered as a health problem all over the world. Nowadays, vitamin D deficiency has involved more than half of people (1). Vitamin D plays an important role in calcium metabolism, maintenance of the skeleton, in control of cell proliferation and differentiation and in immunity (2). Recently, it has been shown that vitamin D deficiency may be related to serum glucose, serum insulin, and insulin sensitivity, hypertension, hyperlipidemia, and obesity (3). These factors are linked to increased risks of serious health complications such as type 2 diabetes, CVD, stroke, and kidney failure.

Base on several studies ,obese and overweight people mostly have a lower levels of vitamin D than those who have less body fat (4). Some studies suggested that obesity increased risk of vitamin D deficiency. It was seen that there is an inverse association among vitamin D with body mass index (BMI) and waist circumference (WC) although the interventional study with vitamin D supplementation alone is rare (3, 5-9).

In addition, observational and intervention studies have demonstrated that high levels of vitamin D are associated with a favorable lipid profile, whereas low levels of vitamin D are associated with an atherogenic lipid profile. However, the results of clinical studies are inconclusive and the possible mechanisms linking dietary vitamin D status with them remain undefined. As regard the prevalence of vitamin D deficiency (defined as levels  $< 75$  nmol/L or  $< 30$  ng/mL) in some region of Iran was estimated approximately 81/3% (10). The study about vitamin D supplementation, blood pressure and lipid profile are controversial, thus in this study, we tried to perform an assessment about the effects of vitamin D supplementation on anthropometric indices, and lipid profile on obese and overweight women.

**Subjects:**

This double blind clinical trial study was performed on overweight and obese women in Isfahan Endocrine and Metabolism center and female students of Isfahan University of medical science. Convenient method was used to enroll participants to the study. The following inclusion criteria was used to select participants: 20–40-year females, BMI higher than 25 (obese and overweight), no-smoking, no history of diabetes, no hyper and hypothyroidism, no participation in other weight reduction programs, no weight reduction during two past month, regular menstrual cycle and no pregnancy. The questionnaire was included information about demographic characteristics such as location, education level, marital status and the number of pregnancy and children. In addition, physical activity, the duration and times of sleep, consumption of supplements, and being on a special of diet were assessed. After giving general overview about this study all subjects provided informed written consent.

### **Study design:**

The aim of this double blind clinical trial study was to evaluate the effect of vitamin D supplementation on anthropometric indices, blood Pressure, lipid profile in 20-40 year obese and overweight women in Isfahan Iran. The enough sample size was 25 person in each group that calculated according to the following formula  $N = (z_1 + z_2)^2 2s^2/d^2$ . In this formula  $\alpha$  was considered 0.05 and  $\beta$  was 80%. So, we recruited 57 persons to compensate potential losses during 6 weeks at follow up. After that, subjects were randomly assigned into two groups (intervention and control) and received vitamin D supplements and placebo, respectively. The participants and laboratory staffs did not aware of the group assignment. The individual continued their usual diet during study. The intervention follow up was 6 weeks that began from 21 May to 5 July 2013. At the first visit, we gave 6 pearls of vitamin D supplements to intervention group and 6 pearls of

placebo to the controls and we asked them to eat one per week. Supplements made in Zahravi pharmaceutical company, Tabriz, Iran. The dozens of supplements were 50000 IU and placebo had the same shape, color, and packaging with given supplement. In addition, at the first meeting, food record has been explained to the subjects and they were asked to record it for three days including one-weekend and two-week days, and expert nutritionist reviewed the dairies. The food record dairies were analyzed by the Nutritionist IV software (version 7.0; N-Squared Computing, Salem, OR, USA). In addition, the subjects were asked to report their physical activity during one selected week. In addition, participants recorded their daily amount of sun exposure from sunrise until sunset. The levels of total cholesterol (TC), triglyceride (TG), low- density lipoprotein cholesterol (LDL-c), high- density lipoprotein cholesterol (HDL-c), serum vitamin D level, height, weight (wt), WC, HR, and BMI were measured at the beginning and the end of study. Height was measured by tape without shoes, nearest to the 0.1 cm and a Beshel model digital scale (Germany) was used to measure weight nearest to the 0.1 kg while subjects wore light clothing with no shoes. BMI was calculated with this formula,  $BMI = \text{weight (Kg)} / \text{height}^2 \text{ (m)}$ . BMI between 24.9-29.9  $\text{Kg/m}^2$  was defined as overweight and more than 29.9  $\text{kg/m}^2$  was defined as obese. Waist circumference was measured at the narrowest level and that of the hip at the maximum level over light clothing, using an unstretched tape meter, without any pressure to body surface and measurements were recorded to the nearest 0.1 cm, as reported earlier and WHR was calculated by dividing waist circumferences by hip circumferences.

**Biochemical analysis:**

Blood samples were taken in a sitting position following 12-14 hour overnight fasting before and after the intervention. Lipid profiles were measured by biochemical auto analyzer A15 with Biosystem kit (made by Spain). The enzyme-linked immunosorbent assay (ELISA) method was used to determine concentration of serum vitamin D(11).

### **Statistical methods:**

All data are presented as mean  $\pm$  SE throughout the paper. Normal distributions of all variables were analyzed by the Kolmogorov-Smirnov test and by evaluating the histogram curves. Kruskal-Wallis test was used for comparing ordinal or non-normal variables. Independent-samples t-test was performed to compare the means of variable between groups and paired-samples t-test was used to compare means before and after intervention. The data were analyzed with SPSS software version 20. The significance was considered 0.05.

### **Result:**

From 75 potentially eligible participants, 6 persons were excluded due to personal reasons, 8 persons had normal serum levels of vitamin D, 5 blood specimens were devastated due to the laboratory personnel mistake. We could not take blood from three participants because of high weight. So, they were eliminated. Finally, we had 53 subjects that 26 of them were assigned to intervention group and 27 of them were entered in control group. The baseline characteristics of 53 obese and overweight women were shown in table 1. Anthropometric variables of participants were presented in table 2. According to data, there were no significant differences in baseline anthropometric variables between intervention and control groups except WC which was significantly higher ( $p=0.04$ ) in intervention group. The analysis shown that in intervention group

the means of weight, BMI, and WC were reduced significantly ( $73.2\pm7.6$  to  $71.6\pm7.7$ ,  $28\pm2.7$  to  $27.2\pm2.8$ ,  $90.4\pm7.2$  to  $88\pm7.5$ , respectively. ( $p < 0.001$ ), but WHR ( $0.85\pm0.05$  to  $0.84\pm0.06$ ) did not change significantly (table 2). As it has shown in table 3 there were no differences in means of dietary energy, macro and micronutrient such as vitamin D of participants between two groups. Biochemical variables were reported in table 4. The assessment of biochemical markers (HDL-c, LDL-c, TC, TG, FBS, Ins, HOMA-IR) in two groups shown that there were no significantly differences in all of the biochemical variables ( $p > 0.05$ ), except for the vitamin D that was  $21.9\pm6.5$  in intervention and  $18.1\pm4.8$  in control groups ( $p < 0.01$ ). The mean of differences in anthropometric and laboratory variables were presented in table 5. After calculating the mean of differences in two groups, cleared that intervention with the vitamin D ( $p < 0.001$ ) decreased the means of weight ( $1.6\pm1.3$ ), BMI ( $0.6\pm0.5$ ), WC ( $2.3\pm1.1$ ) and increased the mean of vitamin D  $62\pm29$  ( $p < 0.001$ ). Also, after adjusting for age the means of the vitamin D was significant ( $83.49\pm5.43$ ,  $34.2\pm5.33$   $p=0.001$ ).

Table 1: Baseline characteristics of the participants<sup>†</sup>

Parameter	Intervention (n=260)	Control (n=27)	P*
Age	29.1±9.6	26.9±9.1	0.4
The number of children	1.0±1.3	0.48±0.93	0.06
Job (%)			
Homeworker	30.80	25.90	0.54
Student	53.80	66.70	
Employee	15.40	7.4	
Marital status (%)			
Single	53.80	33.3	0.13
Married	46.20	66.70	
Education level (%)			
Less than high school	3.8	11.10	0.24
High school and higher	46.2	18.50	
College education and higher	50.00	70.40	
Physical activity (min/week)	874.8±697.1	604.5±643.4	0.14
Sun exposure (min/day)	49.6±40	61.5±49.3	0.34

\* $P < 0.05$  is significant; obtained from independent  $t$ -test and  $\chi^2$ , <sup>†</sup>Values are mean±SD. SD=Standard deviation

Table 2: Anthropometric variables of the participants

Variables	Intervention	Control	<i>P</i> *:‡
Weight (kg)			
Baseline	73.2±7.6	70.3±9	0.02
End	71.6±7.7	70.3±9	
<i>P</i> *	0.001	0.81	
Height	162±7	158.8±6	0.8
BMI (kg/m <sup>2</sup> )			
Baseline	28±2.7	27.8±2.6	0.91
End	27.2±2.8	27.8±2.7	0.4
<i>P</i> *	0.001	0.81	
WC (cm)			
Baseline	90.4±7.2	86±8	0.04
End	88±7.5	86.3±8.5	0.42
<i>P</i> *	0.001	0.27	
WHR			
Baseline	0.85±0.05	0.81±0.05	0.4
End	0.84±0.06	0.82±0.06	0.4
<i>P</i> *	0.23	0.44	
SBP (mmHg)			
Baseline	112.7±8.5	112.5±5	0.9
End	112.3±10	112±6.5	0.8
<i>P</i> *	0.8	0.6	
DBP (mmHg)			
Baseline	80±6.5	78.5±8.5	0.4
End	78±5	76±6	0.2
<i>P</i> *	0.15	0.17	

\**P*<0.05 is significant, †Values are mean±SD, ‡For comparison of between-group differences by an independent *t*-test. BMI=Body mass index, WC=Waist circumference, WHR=Waist to hip ratio, SBP=Systolic blood pressure, DBP=Diastolic blood pressure, SD=Standard deviation

Table 3: Dietary intake of participants before study†

Nutrient	Intervention	Control	<i>P</i> *:‡
Energy (kcal)	2096±6.3	2117±661	0.9
Carbohydrate (g)	292±107	300±157	0.8
Protein (g)	83±36	102.5±89	0.5
Fat (g)	73.5±31	78.5±77	0.3
Saturated fatty acid (g)	20±8	24.5±23	0.4
Polyunsaturated fatty acid (g)	21.5±12	22±15	0.8
Monounsaturated fatty acid (g)	32.2±118	42±214	0.7
Fiber soluble (g)	0.5±0.2	0.8±1.5	0.3
Fiber insoluble (g)	4.5±8	6±12.5	0.5
Calcium (mg)	841±363	899±646	0.7
Vitamin D (Ug)	1.4±1.9	1.3±2	0.93

\**P*<0.05 is significant, †Values are mean±SD, ‡For comparison of between-group differences by an independent *t*-test. SD=Standard deviation

Table 4: Biochemical variables in participants†

Variables	Intervention	Control	P*‡
TC(mg/dl)			
Baseline	184.3±37	188.7±42.5	0.7
End	184±34	176.5±28	0.4
P	0.9	0.07	
LDL (mg/dl)			
Baseline	89.5±25	91.4±27	0.8
End	92.7±25.5	87.5±21.2	0.4
P	0.3	0.3	
HDL(mg/dl)			
Baseline	42.8±11.5	48.7±16	0.1
End	42.8±8.7	44.3±10	0.5
P	0.1	0.7	
TG (mg/dl)			
Baseline	118±90	109.5±56	0.7
End	120.5±111	100±48	0.4
P			
Vitamin D (nmol/l)			
Baseline	22±6.5	18±5	0.01
End	84±30.5	34±24	0.001
P	0.001	0.001	

\*P<0.05 is significant, †Values are mean±SD, ‡For comparison of between-group differences by an independent t-test for comparison of within-group differences by an paired t-test. TC=Total cholesterol, TG=Triglyceride, LDL-C=Low-density lipoprotein cholesterol, HDL-C=High-density lipoprotein cholesterol, SD=Standard deviation,

Table 5: The mean of differences in anthropometric and biochemical variables

Variables	(n=26)	(n=27)	
Weight (kg)	-1.6±1.3	0.05±1	0.001
BMI	-0.61±0.5	0.02±0.5	0.001
WC (cm)	-2.3±1	0.3±1.5	0.001
WHR	0.01±0.04	-0.0008±0.03	0.22
HDL-C (mg/dl)	0.003±8	-4.4±12.5	0.13
LDL-C (mg/dl)	3.17±17.5	-4±19	0.17
TC (mg/dl)	-0.3±26	-12.2±33.5	0.15
TG (mg/dl)	2.5±48.5	-9±34.5	0.3
Vitamin D	62±29	15.7±22	0.001
SBP (mmHg)	-0.5±8	-0.75±7	0.9
DBP (mmHg)	-2.3±8	-2.6±9.6	0.9

\*P<0.05 is significant, †Values are mean±SD, ‡For comparison of between-group differences by an independent t-test. TC=Total cholesterol, TG=Triglyceride, LDL-C=Low-density lipoprotein cholesterol, HDL-C=High-density lipoprotein cholesterol, SBP=Systolic blood pressure, DBP=Diastolic blood pressure, , BMI=Body mass index, WC=Waist circumference, WHR=Waist to hip ratio

## Discussion:

The findings of this double blind clinical trial study in obese and overweight women aged 20-40 year showed that supplementation of the vitamin D with doses 50000 IU for 6 weeks reduced significantly the mean of BMI , weight , WC and on the other hand increased significantly the level of vitamin D in comparison with the control group. However, there were no significant effect of the vitamin D on other factors such as WHR, DBP, and lipid profiles. In addition, the level of vitamin D increased in control group. One of the possible causes of this increase can be attributed to the change of season with different amount and intensity of the sun exposure.

Previous studies had shown that the vitamin D deficiency is more prevalent in obese people and there were an inverse association between vitamin D, BMI and WC (2-8, 12-17). Goupta et al showed that 1 kg/m<sup>2</sup> increase in BMI were associated with significantly reduced in vitamin D level( 42% ng /ml)(18). In another study, there was a significant inverse relationship after adjusting all confounding that associated with vitamin D and BMI (19). However conflicting results has been seen (2, 5, 20). Such as a study on Iranian 20-64 yr with BMI 24.2±3.8 (57% female) which had not shown significant association between the level of vitamin D and BMI. Probably its main reason was BMI, which was 24.2 and in the normal range. In addition it could be another reason that only 48% of subjects had vitamin D deficiency (5). In some studies the inverse association between vitamin D and WC has been seen (18, 21). In Seo study only this association between vitamin D and WC has been seen in women. The reason of the vitamin D deficiency in obesity has not certainly cleared but some mechanisms has proposed for the relationship between vitamin D and obesity: trapped of the vitamin D in adipose tissue that makes less bioavailability for convert to the form of 1,25-(OH)<sub>2</sub>D<sub>3</sub> (22) .

In this study we could not find any role of vitamin D on the lipid profile such as triglyceride , TC, HDL-C, and LDL-c. Result of this study were approved by previous studies (24-26). In Moghassemi et al of Iran after 12 weeks supplementation of the vitamin D could not show any significant differences in women's lipid profile (24). In a randomly clinical trial on women have not been found any changes in lipid profile that researchers stated it was because of insufficiently study duration and dose of the vitamin D (25). In addition some studies such as WHI (Women Health Initiative) that had longer duration and dose of the vitamin D were 200 IU that take it twice a week for seven years has not found changes in lipid profile (26). In several studies, similar results were obtained (8,18, 23) . But some studies have found inverse results such as Hyoungh-Jun et al that after supplementation of the vitamin D only HDL-c was reduced significantly (23). in another study LDL-c and TG decreased significantly (27) but HDL-c increased significantly (28). In a similar study after consuming the supplementation of vitamin D with dozes 300IU/d for 3 years, LDL-c and TG increased significantly but TC and HDL-C reduced significantly(29) Meta-analysis was conducted on the effects of vitamin D supplementation on lipid profile shows that,there are only significant relationship on LDL that after the intervention it was increased (25). In some studies have reported that improved these factors may be due to weight reduction.

We have not seen significantly relationship between supplementation of the vitamin D and blood pressure in our study .In a clinical study in Germany supplementation of the vitamin D with dozes 100000 IU did not cause any changes in blood pressure (30). In a meta-analysis that included of 10 interventional studies, after supplementation of the vitamin D no significant effects found in systolic and diastolic blood pressure (31). As well as several other studies have not reported the effect of vitamin D on blood pressure (23, 32, 33). However, a

study has reported an inverse relationship between vitamin D levels and systolic blood pressure in men (7), but probably its main reason was subjects age because the aim society in this study were the subjects with aged higher than 65 year and mostly had a high blood pressure but participants in our study were subjects 20-40 year that mostly had a normal blood pressure. Another possible reason was the difference in gender. The possible mechanisms that suggested for the effect of vitamin D on blood pressure are regulating renin- angiotensin system, suppressing the spread of proliferation of vascular smooth muscle cells, improving insulin resistance, modifying extended dependent cells to endothelium and inhibiting of anticoagulant activity and hypertrophy of myocardial cells by vitamin D (34) .Finally, a number of limitations need to be considered: first, the short duration of the study, second, no dietary assessment at the end of study, and third investigation in different seasons so different sun exposure duration that can influence on serum vitamin D level. So, more studies with higher sample size, longer duration of intervention, in various geographic regions with different dozes is suggested.

### **Conclusion:**

The purpose of the current study was to determine the effects of vitamin D supplementation on body weight, waist circumference (WC), waist to hip ratio (WHR), and lipid profile among obese and overweight women. The evidence of this study suggests, which supplementation of the vitamin D with dozes 50000 IU/w for 6 weeks in obese and overweight women aged 20-40 year lead to reduce in the BMI, weight and WC significantly whilst this study did not confirm the effect of vitamin D supplementation on lipid profile, thus the assessment of vitamin D status in obese persons, is suggested.

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## **Conflict of interest:**

The authors declare that there is no conflict of interest.

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