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Effect of Vitamin D deficiency on Lipid Profile

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Abstract: The purpose of this study is to investigate the effect of vitamin D deficiency on lipid parameters; cholesterol, triglycerides, low density lipoprotein (LDL), and high density lipoprotein (HDL). Serum level of vitamin D and the lipid parameters were determined in 127 subjects attending private community lab in eastern Amman province, using commercially available kits. Deficiency and insufficiency of vitamin D were 36.2%, 29.9%, respectively. Serum level of cholesterol, triglycerides, and LDL in deficient and insufficient vitamin D subjects were significantly increased, while HDL level was decreased, P-value <0.05. Serum levels of lipid profile and vitamin D in each of the control, insufficient , and deficient groups were all normally distributed due to the fact that P-value is greater than 0.05. Interval plot analysis and One-way ANOVA analysis revealed a significant effect of vitamin D insufficiency or deficiency on serum level of cholesterol, triglycerides, and LDL and increases the levels more than the double. Two samples T-test for every lipid parameter analysis related to subjects in the sufficient, insufficient and deficient vitamin D groups confirm our hypothesis on the effect of vitamin D deficiency on increasing the levels of cholesterol, triglycerides, and LDL and decreasing the level of HDL.

Keywords: Vitamin D, Cholesterol, Triglycerides, Low Density Lipoprotein, High Density Lipoprotein

1. Introduction

Dyslipidemia is characterized by hypertriglyceridemia, hypercholesterolemia, reduced high density lipoprotein, and elevated low density lipoprotein. Dyslipidemia is considered as a key factor associated with the increased risks of several cardiovascular disease [1], which is considered as a major causative factor for death [2]. The therapeutic interventions for lowering level of cholesterol can also decrease the mortality and morbidity due to cardiovascular diseases. Some research studies have also demonstrated a link between dyslipidemia and decreased concentration of vitamin D [3]. Vitamin D is one of essential fat soluble vitamin, which performs many functions in the human body. The prime source providing vitamin D to human is exposure to sunlight [4]. The skin contain 7-dehydrocholesterol which after absorption of the ultraviolet B radiation is converted to previtamin D3 and after that it is hydroxylated into 25(OH)D and then converted into 1,25-dihydroxyvitamin D3 with the help of hydroxylases found in kidneys and livers. The sources of vitamin D are oral supplements and diet. Bone metabolism and regulation of calcium are important physiological functions of vitamin D [5]. In addition, vitamin D is also considered as a modulator of immune system functions, anti-inflammatory activity, reduce resistance of insulin, and suppress rennin-angiotensin system. In addition, it is stated by several research studies that deficiency of vitamin D is significantly associated with some cardiovascular diseases. The predefined aim of this research study is to determine the effect of vitamin D deficiency or insufficiency on serum levels of cholesterol, triglcerides, LDL, and HDL. The specific objectives of this research study is to demonstrate the effect of low levels of vitamin D on lipid profile.

2. Literature Review

The importance of vitamin D is described by several research studies and some of researcher have also focused on determining vitamin D impact on the lipid profile of a person. It is suggested by some researchers that concentration of vitamin D has a strong association with the dyslipidemia and risks of different cardiovascular disorders [1-7]. As stated in the literature, deficiency in vitamin D is significantly associated with prevalence of some cardiovascular disease as well as dyslipidemia. It has been demonstrated by other researchers that the decreased level of 25(OH)D is associated independent with increased mortality rates of the patients having cardiovascular disease [8]. Some other research studies have also presented the association with deficiency of vitamin D and dyslipidemia and several cardiovascular diseases [9, 10]. Other research studies have also presented a significant association between dyslipidemia and decreased level of vitamin, yet outcomes of most of these research studies were insignificant [8-10]. Some other researchers have highlighted the significance of increasing blood level of vitamin D to reduce the risks of different dyslipidemia associated cardiovascular diseases such as stroke, myocardial infarction, and hypertension [9, 11]. The abnormalities of lipoproteins can be associated with increased levels of LDL-C, TG, TC, or reduced levels of HDL-C and in case of vitamin D deficiency, risks of these abnormalities are increased to a high level. The increased level of these lipoproteins has a significant association with the cardiovascular morbidity. Yet, there is limited research demonstrating the association of vitamin D deficiency and lipid profile induced cardiovascular diseases [11]. However, some researchers have provided the association between the level of lipids in serum and levels of 25(OH)D. The outcomes of a cross-sectional study that was carried out to determine the relationship between the levels of vitamin D and lipoproteins have revealed positive outcomes [12]. A research study had presented that the levels of serum 25(OH)D have a positive relationship with the levels of LDL-C, TC, and HDL-C, and negative association between the levels of 25(OH)D and serum levels of TG. However, the outcomes obtained from another study were completely different and suggested a negative association between levels of TG, TC, and LDL-C, while the relationship between HDL-C and 25(OH)D was found positive and significant [13].

3. Subjects and Methods

3.1. Subject

Serum level of Vitamin D and lipid profile were assesed in blood samples taken from 127 subjects attending the lab for routine blood testing. Criteria for dyslipidemia patients weather they are taking lipid lowering medications or not, and if the patient had type 2 diabetes, the above criteria and the presence of LDL-c levels > 65mg/dl are mandatory. None of the subjects are taking vitamin D supplements. Informed consent was obtained from all individual participants included in the study. According to serum level of vitamin D, these subjects were categorized into three groups; forty three sufficient vitamin D subjects (>30ng/ml), (Control group 1), thirty eight insufficient (15-30ng/ml) (group 2), and forty six deficient (<15ng/ml) (group 3).

3.2. Biochemical Analysis

Blood specimens were obtained after overnight fasting in plain tubes, and have been frozen at -20°C till annalysis. The lipid profile included total cholesterol, triglycerides, and HDL-c which were measured by commercially available kits for all participants. LDLc was calculated using Friedewald's equation when triglycerides did not exceed 300 mg/dl. Vitamin D was determined by radioimmunoflourescence commercially available kits (TOSOH ST AIA-PACK).

3.3. Statistical Analysis

Data were analyzed using the MiniTab software. Normality of data distribution was evaluated using Kolmogorov-Smirnov in the transversal analysis. The relationship between qualitative variables was assessed using Chi-square test and quantitative variables were analyzed by means of Pearson's or Spearman's correlation coefficient. Differences between groups were evaluated by T-test, Mann–Whitney test and Interval Plot Analysis. The level of statistical significance Alpha (α) = 0.05.

4. Results

4.1. Lipid Profile and Vitamin D Status in Deficient and Insufficient Groups

As shown in Table 1, the frequency of vitamin D sufficient group (control), insufficient vitamin D group, and deficient group was 43 (33.9%), 38 (29.9%), and 46 (36.2%), respectively. In the insufficient vitamin D group, the concentration of vitamin D (ng/ml), glucose (mg/dl), cholesterol (mg/dl), triglycerides (mg/dl), HDL (mg/dl), and LDL (mg/dl) are 18.8±2.44, 213.8±99.6, 244.3±40.88, 265.6±128.4, 46.17±13.73, and 145.02±40.6, while in the deficient group the concentrations are; 11.26±1.8, 215.2±80.1, 239.7±65.51, 246±148.6, 48.6±18.66, and 142.81±47.69, respectively. (Table 2, Figure 1). The difference in mean of glucose, cholesterol, triglycerides, LDL, and HDL between contols and each of insufficent and deficient groups is significant, P<0.05 as presented in Table 2 and figure 1. There is no significant difference in serum levels of vitamin D, glucose, total cholesterol, triglycerides, HDL, or LDL, between the insufficient vitamin D and deficient groups, P>0.05.

Table 1. *Status of vitamin D in a random selected sample of 127 participants in eastren Amman province, Jordan.*

Groups of vitamin D	Number, n	Percentage,%
Group 1: Sufficient vitamin D (>30ng/ml)	43	33.9
Group 2: Insufficient (15-30ng/ml)	38	29.9
Goup 3: Deficient (<15ng/ml)	46	36.2

Table 2. *Serum levels of vitamin D , glucose, and lipid profile in Group I: (Sufficient Vitamin D , n=43), Group II (Insufficient Vitamin D , n=38), and Group III (Deficiency Vitamin D , n=46).*

| Tested parameters	Group I: Sufficient Vitamin D (n=43)		Group II: Insufficient Vitamin D (n=38)		Group III: Deficiency Vitamin D (n=46)	
	Mean	Stand. Dev.	Mean	Stand. Dev.	Mean	Stand. Dev.
Vitamin D (ng/ml)	42.14	9.47	18.8	2.44	11.26	1.8
Glucose (mg/dl)	92.23	9.43	213.8	99.6	215.2	80.1
Cholesterol (mg/dl)	148.1	15.25	244.3	40.88	239.7	65.51
Triglyceride (mg/dl)	143.5	25.17	265.6	128.4	246	148.6
HDL (mg/dl)	63.33	12.84	46.17	13.73	48.6	18.66
LDL (mg/dl)	56.02	10.19	145.02	40.6	142.81	47.69
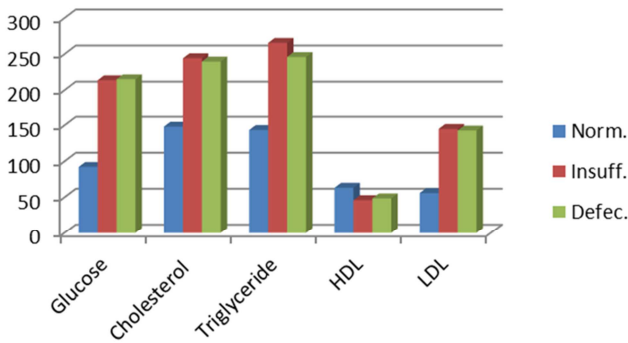
Figure 1. *Serum levels of glucose and lipids panel in suffient control group, n=43 (Norm) , insufficient vitamin D group, n=38 (Insuff.), and vitamin D deficient group, n=46 (Defec.).*

4.2. Normality Testing

Group 1 (sufficient vitamin D with normal lipid profile) data, group 2 (insufficient vitamin D with abnormal lipid profile), and group 3 (deficient vitamin D with abnormal lipid profile) all follow normal distribution, P-vale > 0.05. (Figures 2, 3, and 4)
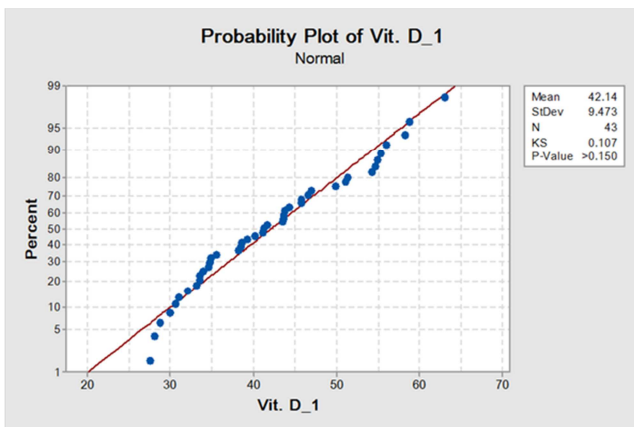

Figure 2. *Distribution of serum levels of vitamin D in group I - normal lipids, normal vitamin D in 43 subjects, mean=42.14 ng/ml, standard deviation=9.47, P value >0.15.*
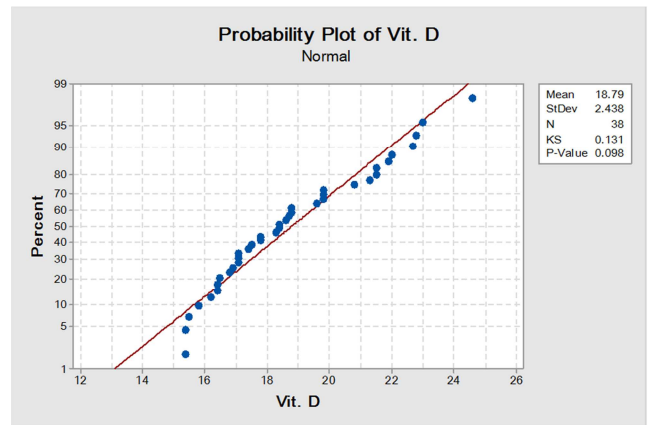

Figure 3. *Distribution of serum levels of vitamin D in group II (insufficient vitamin D) in 38 subjects, mean= 18.79 ng/ml, standard deviation=2.44 , P value >0.098.*
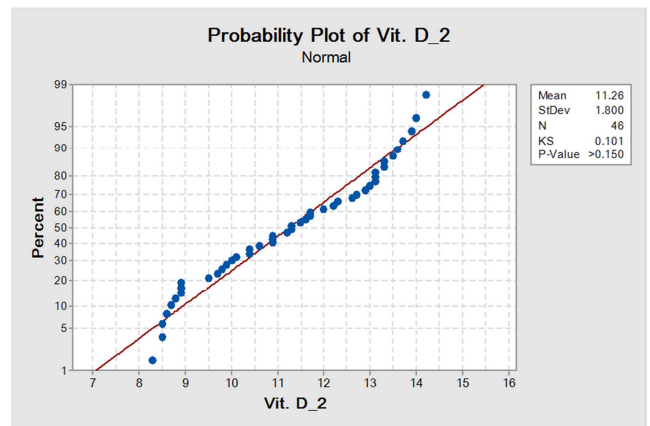

Figure 4. *Distribution of serum levels of vitamin D in group III (deficient vitamin D) in 46 subjects, mean= 11.26 ng/ml, standard deviation=1.8, P value >0.15.*

4.3. Comparison Between Lipid Parameters for Different Groups of Vitamin D and Analysis of Variances

The effect of vitamin D deficiency or insufficiency on on the mean of different variables (glucose, TC, TG, LDL, and HDL) was evaluated by using interval plot annalysis and one

way ANOVA . Elevated levels of glucose, total cholesterol, triglycerides, and LDL, and low level of serum HDL were observed. Glucose levels in vitamin D deficient group, normal vitamin D group, and in vitamin D insufficient group was 221.7±105.6 , 95% CI (197.9; 245.5), 92.23± 9.43, 95% CI (69.30; 115.17) 215.2± 80.1 , 95% CI (193.1; 237.4) , respectively. (figure 5).
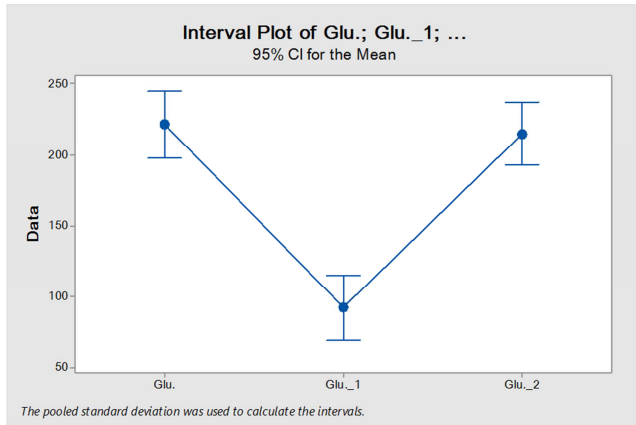

Figure 5. Interval plot analysis to compare between glucose levels for different groups of Vitamin D, Glu_1 (group I; sufficient control group, n=43), Glu_2 (group II; insufficient vitamin D group, n=38), Glu (group III; deficient vitamin D group, n=46).

Total cholesterol levels in vitamin D deficient group, normal vitamin D group, and in vitamin D insufficient group was 262.2± 68.8, 95% CI (244.8; 279.5), 148.05± 15.27, 95% CI (131.31; 164.78), 239.65± 65.51, 95% CI (223.47; 255.83) , respectively.(figure 6).
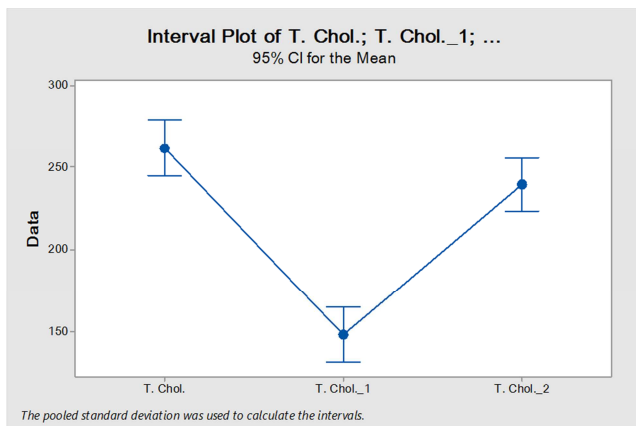

Figure 6. Interval plot analysis to compare between total cholesterol levels for different groups of Vitamin D, T. Chol_1 (group I; sufficient control group, n=43), T. Chol_2 (group II; insufficient vitamin D group, n=38), T. Chol. (group III; deficient vitamin D group, n=46).

Triglycerides levels in vitamin D deficient group, normal vitamin D group, and in vitamin D insufficient group was 276.1 ± 136.9 , 95% CI (239.2; 313.0), 143.49± 25.17, 95% CI (107.92; 179.06), and 246.0 ± 148.6, 95% CI (211.6; 280.3), respectively, Figure 7.
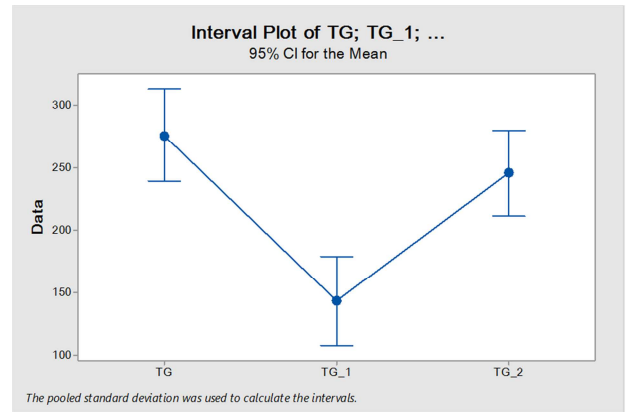

Figure 7. Interval plot analysis to compare between triglycerides levels for different groups of Vitamin D, TG_1 (group I; sufficient control group, n=43), TG_2 (group II; insufficient vitamin D group, n=38), TG (group III; deficient vitamin D group, n=46).

High density lipoprotein (HDL) levels in vitamin D deficient group, normal vitamin D group, and in vitamin D insufficient group was 47.13± 15.00, 95% CI (42.20; 52.07), 63.33± 12.84, 95% CI (58.57; 68.09), and 48.60 ± 18.66 , 95% CI (44.00; 53.21) , respectively, Figure 8.

Figure 8. Interval plot analysis to compare between HDL levels for different groups of Vitamin D, HDL_1 (group I; sufficient control group, n=43), HDL_2 (group II; insufficient vitamin D group, n=38), HDL (group III; deficient vitamin D group, n=46).
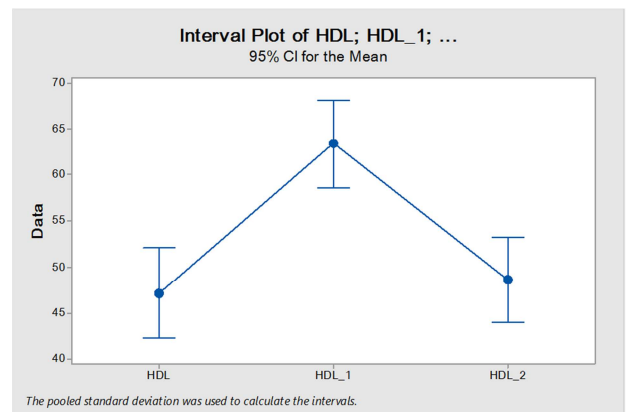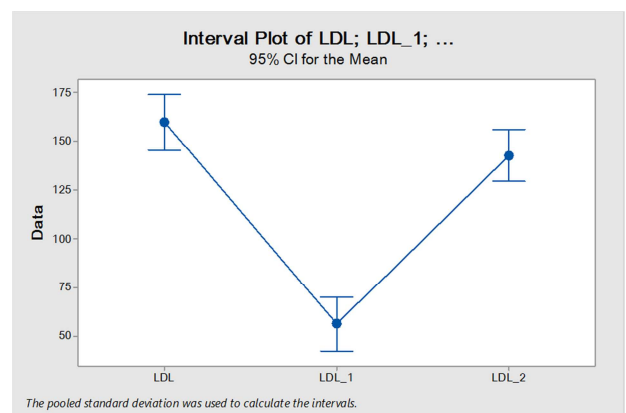

Figure 9. Interval plot analysis to compare between LDL levels for different groups of Vitamin D, LDL_1 (group I; sufficient control group, n=43), LDL_2 (group II; insufficient vitamin D group, n=38), LDL (group III; deficient vitamin D group, n=46).

Low density lipoprotein (LDL) levels in vitamin D deficient group, normal vitamin D group, and in vitamin D insufficient group was 159.83 ± 62.81, 95% CI (145.60; 174.06), 56.02 ± 10.19 , 95% CI (42.29; 69.74), and 142.81 ± 47.69 , 95% CI (129.54; 156.08), respectively, Figure 9.

4.4. Testing of Hypothesis

A complete testing of hypothesis was conducted to check the effect of different levels of concentration of vitamin D on every lipid parameter concentration.

The testing of hypothesis was conducted on the mean of every parameter compared to other for different levels of vitamin D. The level of significant used in these tests was 0.05, and if the p-value < 0.05, then the null hypothesis will be rejected. Rejecting the null hypothesis means that the two means are different, otherwise the means are almost equal. The estimated difference in glucose (Glu) in normal vitamin D concentration (group I) , insufficient (group II) , and deficient (group III) is 129.5 with 95%CI (95.6; 163.4) P=0, 6.5 with 95%CI (-34.3; 47.2) P=0.753, and -123with 95%CI (-147.0; -99.1) P=0 , respectively. Accordinly null hypothesis (H_0) is rejected, fail to reject, and rejected in group I, group II, and group III, respectively, Table 3. The estimated difference in total cholesterol in normal vitamin D concentration (group I) , insufficient (group II) , and deficient (group III) is 114 with 95%CI (91.7; 136.6) P=0, 22.5 with

95%CI (-6.4; 51.5) P=0.125, and -91.6 with 95%CI (-111.56; -71.65) P=0 , respectively. Accordinly null hypothesis (H_0) is rejected, fail to reject, and rejected in group I, group II, and group III, respectively, Table 3. The estimated difference in triglycerides (TG) in normal vitamin D concentration (group I) , insufficient (group II) , and deficient (group III) is 132.6 with 95%CI (88.3; 177.0)P=0, 30.2with 95%CI (-31.1; 91.4)P=0.33, and -102.5with 95%CI (-147.2; -57.7) P=0 , respectively. Accordinly the null hypothesis (H_0)is rejected, fail to reject, and rejected in group I, group II, and group III, respectively, Table 3. The estimated difference in high density lipoprotein (HDL) in normal vitamin D concentration (group I) , insufficient (group II) , and deficient (group III) is -16.2 with 95%CI (-22.32; -10.08) P=0, -1.47with 95%CI (-8.69; 5.75)P=0.69, and 14.73 with 95%CI (8.01; 21.45) P=0 , respectively. Accordinly null hypothesis (H_0) is rejected, fail to reject, and rejected in group I, group II, and group III, respectively, Table 3. The estimated difference in low density lipoprotein (LDL) in normal vitamin D concentration (group I) , insufficient (group II) , and deficient (group III) is 103.8with 95%CI (83.5; 124.1) P=0, 17.0 with 95%CI (-7.2; 41.3) P=0.166, and 86.8 with 95%CI (72.32; 101.26) P=0 , respectively. Accordinly null hypothesis (H_0) is rejected, fail to reject, and rejected in group I, group II, and group III, respectively.

Table 3. A complete testing of hypothesis to check the effect of different levels of concentration of vitamin D on every lipid parameter concentration.

No.	Null Hypothesis	Estimated diff.	95% C.I.	P-Value	Decision
1	M (Glu.)- μ (Glu._1)= 0	129.5	(95.6; 163.4)	0.000	Reject H_0
2	μ (Glu.) - μ (Glu._2)= 0	6.5	(-34.3; 47.2)	0.753	Fail to Reject H_0
3	μ (Glu._1) - μ (Glu._2) = 0	-123	(-147.0; -99.1)	0	Reject H_0
4	μ (T. Chol.) - μ (T. Chol._1) = 0	114	(91.7; 136.6)	0	Reject H_0
5	μ (T. Chol.) - μ (T. Chol._2) = 0	22.5	(-6.4; 51.5)	0.125	Fail to Reject H_0
6	μ (T. Chol._1) - μ (T. Chol._2) = 0	-91.6	(-111.56; -71.65)	0	Reject H_0
7	μ (TG) - μ (TG_1) = 0	132.6	(88.3; 177.0)	0	Reject H_0
8	μ (TG) - μ (TG_2) = 0	30.2	(-31.1; 91.4)	0.33	Fail to Reject H_0
9	μ (TG_1) - μ (TG_2) = 0	-102.5	(-147.2; -57.7)	0	Reject H_0
10	μ (HDL) - μ (HDL_1) = 0	-16.2	(-22.32; -10.08)	0	Reject H_0
11	μ (HDL) - μ (HDL_2) = 0	-1.47	(-8.69; 5.75)	0.687	Fail to Reject H_0
12	μ (HDL_1) - μ (HDL_2) = 0	14.73	(8.01; 21.45)	0	Reject H_0
13	μ (LDL) - μ (LDL_1) = 0	103.8	(83.5; 124.1)	0	Reject H_0
14	μ (LDL) - μ (LDL_2) = 0	17.0	(-7.2; 41.3)	0.166	Fail to Reject H_0
15	μ (LDL_2) - μ (LDL_1) = 0	86.8	(72.32; 101.26)	0.000	Reject H_0

5. Discussion

Our study demonsrated that 66% of the subjects are vitamin D insufficient and deficient. This finding is conformed with previous reports [14, 15]. Vitamin D deficiency could be due to different reasons such as; feeding much fiber rich food that affect vitamin D absorbtion, restricted intake of fish and fish oil which is rich in vitamin D, limited exposure to sunlight due to different reasons, having dark skin with melanin that reduces the ability of the skin to synthesize vitamin D, problems in digestive tract due to some diseases that interfer with vitamin D absorption, or due to obesity in which fat cells extract vitamin D from blood.

This study showes a significant increase in the mean total cholesterol, triglycerides, and LDL, and a significant decrease in HDL levels with deficiency and insufficiency of vitamine D compared with normal sufficient vitamin D subjects. Cholesterol level is increased significantly with deficiency and with insufficiency of vitamin D. This finding is in agreement with many reported studied [16-19]. This finding of hypercholesterolemia with hypovitamin D is explained if there was a defect in LDL receptors and thus a defect in cholesterol uptake, so cholesterol level in blood will be increased and vitaminD will be decreased because both of them has a common synthetic pathway and it is reported that LDL cholesterol is a precursr of previtamin D [20-24].

In this study Hypertriglyceridemia was demonstrated with

low serum level of vitamin D in patients with vitamin D deficiency and insufficiency which coincide with other studies [25, 26]. It is reported that vitamin D reduces serum level of triglycerides by increasing serum calcium via intestinal absorption. This calcium reduces the synthesis of triglycerides in the liver and its secretion [27]. Another mechanism is to reduce triglycerides via PTH suppression [28].

As shown in Table II, low level of HDL is observed with low level of vitamin D in the deficient and insufficient vitamin D patients. This finding is similar to what other investigators reported [29, 30].

5.1. Normality Test

This test compares the empirical cumulative distribution function of the sample data with the distribution expected if the data were normal. If this observed difference is sufficiently large, the test will reject the null hypothesis of population normality.

H0: data follow a normal distribution vs H1: data do not follow a normal distribution. As shown in figures 2, 3, and 4, one could conclude that data from normal lipid/sufficient vitamin D, hyperlipidemic/insufficient vitamin D, and hyperlipidemic/deficient vitamin D groups , all follow the normal distribution due to the fact that P-value is greater than 0.05. Therefore we fail to reject the null hypothesis.

5.2. Comparison Between Lipid Parameters for Different Groups of Vitamin D and Analysis of Variances

Our data show that the mean level of the glucose (figure 5), cholesterol (figure 6), triglycerides (figure 7), and LDL (figure 9), for the control group of sufficient vitamin D /nomolipids is lower than the insufficient vitamin D/hyperlipidmic and deficient vitamin D/hyperlipidimic groups. It is concluded that insufficiency of vitamin D or deficiency has a significant effect on the glucose, cholesterol, triglycerides, and LDL levels and it will increase them to more than the double. For HDL, it is noted from (figure 8) that the mean of the HDL for sufficient vitamin D /nomolipids group is higher than insufficient vitamin D/hyperlipidimic and deficient vitamin D/hyperlipidimic groups. This means that the effect of Vitamin D insufficiency or deficiency has a significant effect on the HDL level and it will decrease it to almost 30%.

5.3. Testing of Hypothesis

A complete testing of hypothesis was conducted to check the effect of different levels of concentration of vitamin D on every lipid parameter concentration (TableIII). The testing of hypothesis was conducted on the mean of every parameter compared to other for different levels of vitamin D. The level of significant used in these tests was 0.05, and if the p-value < 0.05, then the null hypothesis will be rejected. Rejecting the null hypothesis means that the two means are different, otherwise the means are almost equal. It is concluded from Table III that there are differences between the levels of lipid

parameters in normal vitamin D concentration (control) , insufficient vitamin D patients, and deficient vitamin D group. On the other hand, it is noted that there is no differences between the lipid parameters in the insufficient and deficient vitamin D .

6. Conclusion

Vitamin D deficiency and insufficiency have high frequency in the tested sample in eastren province of Amman, Jordan. Dyslipidemia could be a result of vitamin D deficiency and insufficiency. A significant effect of vitamin D insufficiency or deficiency on serum level of cholesterol, triglycerides, and LDL and increases the levels more than the double and decreases the level of HDL. No difference between the lipid profile parameters in the deficient and insufficient vitamin D . In order to understand the relationship between vitamin D and serum lipid profiles, large randomized, controlled studies are required

Ethical approval: "All procedures performed in studies involving human participants were in accordance with the ethical standards of Jordan university of science and technology research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards."

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