The association of coffee consumption rate with serum 25-hydroxyvitamin D, non-HDL levels, and TC/HDL ratio in females with vitamin D deficiency

Maha Habash[1] [ID], Sami Al-shakhshir[1], Mohammad Abusamak[2,3] [ID], Mohammad Yasin Mohammad[1] and Mahmoud AbuSamak[4]

Abstract

Objectives: The purpose of this study was to evaluate the association of coffee consumption rate with serum 25-hydroxyvitamin D, non-high-density lipoprotein cholesterol levels, and total cholesterol to high-density lipoprotein cholesterol ratio in females with vitamin D deficiency.

Methods: This retrospective cross-sectional study was carried out by studying the records of 270 Jordanian females aged 18–65 years with varying degrees of vitamin D deficiency. Following completion of the questionnaire regarding their anthropometric characteristics and coffee consumption rate during the preceding 3 months, the participants were required to provide blood samples for analysis to measure 25-hydroxyvitamin D and lipid profile levels including non-high-density lipoprotein cholesterol and total cholesterol to high-density lipoprotein cholesterol ratio.

Results: The current study demonstrated that coffee consumption rate and vitamin D deficiency were significantly positively connected with the total cholesterol to high-density lipoprotein cholesterol ratio ($p = .003$) in women with vitamin D deficiency. In addition, vitamin D deficiency alone correlated positively with non-high-density lipoprotein cholesterol levels and the total cholesterol to high-density lipoprotein cholesterol ratio ($p = .010$) and ($p = .002$), respectively.

Conclusion: Higher coffee consumption rate among women with vitamin D deficiency significantly elevated total cholesterol to high-density lipoprotein cholesterol ratio that may increase woman's risk of hyperlipidemia.

Keywords

coffee consumption, lipid profile, non-HDL, TC/HDL ratio, VDD

Introduction

Coffee consumption on a regular basis has been shown to lower the risk of type 2 diabetes mellitus (DM), obesity, liver disease, some cancers, Parkinson's disease, and Alzheimer's disease.[1,2] The benefits and risks of coffee consumption in connection to cardiovascular disease (CVD) have been reviewed.[3] Nevertheless, concerning the rate of coffee consumption, the relationship with hyperlipidemia has not yet been resolved. Inconsistent outcomes have been associated with excessive coffee consumption for low-density lipoprotein cholesterol (LDL-C), known

[1]Michael Sayegh Faculty of Pharmacy, Aqaba University of Technology, Aqaba, Jordan
[2]Department of Surgery, School of Medicine, Al-Balqa Applied University, Al-Salt, Jordan
[3]Amman Eye Clinic, Amman, Jordan
[4]Department of Clinical Pharmacy and Therapeutics, Applied Science Private University, Amman, Jordan

Corresponding author:
Mahmoud AbuSamak, Department of Clinical Pharmacy and Therapeutics, Applied Science Private University, Al Arab St. 21, Amman 11931, Jordan.
Email: m_abusamak@asu.edu.jo

as "bad lipoprotein," as well as high-density lipoprotein cholesterol (HDL-C), often described as "good lipoprotein" levels.[4–7] Some prior studies have predominantly attributed the risk of coffee consumption rate (CCR) to boiled rather than filtered coffee.[8,9] However, to address this issue, subtracting HDL from total cholesterol (TC) means the amount of cholesterol incorporated in all lipoproteins recognized to be atherogenic. This measurement is referred to as non-high-density lipoprotein cholesterol (non-HDL-C), and it affords a more accurate evaluation of CVD risk and is a more reliable predictor of CVD and strokes.[10] Furthermore, multiple reports currently suggest that measuring non-HDL-C levels may be more effective than calculating the cholesterol/high-density lipoprotein cholesterol (TC/HDL) ratio.[11] Non-HDL and TC/HDL ratios are strongly correlated with typical CVD factors.[10–12] However, the effects of CCR on certain lipid profile markers, most notably non-HDL-C, remain unknown and the findings of several studies are inconsistent.[5,13–16]

On the other hand, vitamin D deficiency (VDD) is prevalent throughout the Mediterranean region, particularly in Jordan.[17] It is directly associated with a variety of bone diseases, but the non-skeletal disorders, such as cancer, diabetes, CVD, and atherosclerosis, are of significant interest.[18–21] In addition to atherosclerosis,[5] hyperlipidemia is also involved in other diseases, including cancer and diabetes.[22–24] In this context, lower 25-hydroxyvitamin D (25OHD) values were associated with lipid profile observations linked to atherogenic pathogenesis.[25,26] Although vitamin D_3 supplementation has been associated with a decreased risk of CVD in observational studies,[27,28] this association has not been verified in randomized clinical trials (RCTs).[19,29,30] For example, a recent large RCT with a total of 25,871 participants reported mixed evidence[31] and concluded that supplementation with vitamin D_3 did not result in a reduction in the incidence of invasive CVD in men and women aged 55 years or older. Consequently, it is unknown whether CCR may interfere with the therapeutic effect of D3 supplements on hyperlipidemia in people with VDD. Nonetheless, the extent of the effect of CCR on the relationship between 25OHD and non-HDL, especially among women with VDD, has not yet been determined.[19] Therefore, the current study aims to examine the association of CCR and 25OHD levels on non-HDL and TC/HDL ratio in Jordanian women with VDD.

Study design and participants

This retrospective cross-sectional study was carried out at the Applied Science Private University (ASU) by studying the records of related medical research (D+). It has been approved by the Applied Science Private University's Institutional Review Board (ASU-IRB) (protocol number: DRGS-2014-2015-165). Eligible records and samples for 270 Jordanian females from the ASU community aged 18–65 years with varying degrees of VDD at the ASU

were used in this study. D+ research was conducted in accordance with the Declaration of Helsinki and its amendments. A convenient sample of healthy women aged 18–65 years signed a written consent form and completed a telephone-screening questionnaire. Each participant was contacted by telephone and asked to complete a questionnaire that included questions about her anthropometric and clinical features as well as her coffee consumption in the 3 months before study admission, as described in the previous related study.[2]

Following completion of the questionnaire, the participants were required to provide blood samples for analysis at Ibn Al-Haytham Hospital Laboratory in Amman, Jordan, to measure 25OHD levels.

Sample size and categorization

The sample size was calculated based on the same method of calculation that had been used in a previous related study[17] conducted on Jordanian men and women with VDD from ASU community using the research advisor's calculator, assuming 95% confidence and a margin of error of 5%. In the mentioned study, 72% (293 records) of the total number (407 records) recruited to participate in that study were females (72%), among which 23 were excluded because their 25OHD levels were within normal values (≥30 ng/mL).

As illustrated in Table 1, the remaining 270 women who composed the sample of the study participants were divided twice.

First, based on their CCR, the coffee cup was prepared by mixing 6.5–13.0 g of Alameed Turkish coffee with 150–200 mL of boiling water (this was equivalent to 1–2 teaspoons of coffee powder), resulting in 150 mg of caffeine per cup.[32] CCR-based categories were NCC=had no coffee consumption (NCC), (n=102, 37.7%), MCC=had moderate coffee consumption (1–2 cups/day), (n=134, 49.6%), and HCC=had high coffee consumption (≥3 cups/day) (n=34, 12.7%).

Second, the three categories were as follows based on the severity of VDD (serum level of 25OHD less than 30 ng/mL):

SVD=severe VDD (25OHD level <10 ng/mL) (n=127, 47%), DVD=deficiency of 25-hydroxyvitamin D (25OHD level <20 ng/mL) (n=104, 38.5%), and IVD=insufficiency of vitamin D (25OHD level <30 ng/mL) (n=39, 14.5%)

Collection of anthropometric data and clinical measurements

Duration of morning sun exposure, skin color, body mass index (BMI), height (cm), weight (kg), and other anthropometric data were recorded with face-to-face interview

Table 1. Categorization of the participants (n = 270).

Variable	Categories	Frequency	%
Morning sun exposure	Yes	190	70.4
	No	80	29.6
	Total	270	100.0
Skin color	Colored	136	50.4
	White	134	49.6
	Total	270	100.0
Coffee consumption levels	NCC	102	37.8
	MCC	134	49.6
	HCC	34	12.6
	Total	270	100.0
25OHD deficiency levels	SVD	127	47.0
	DVD	104	38.5
	IVD	39	14.5
	Total	270	100.0

NCC: no coffee consumption; MCC: moderate coffee consumption; CCR: coffee consumption rate; HCR: heavy coffee consumption rate; MCR: moderate coffee consumption rate; NCR; no coffee consumption rate; 25OHD: 25-hydroxy vitamin D; SVD: severe vitamin D deficiency; DVD: deficiency of 25-hydroxyvitamin D; IVD: insufficiency of vitamin D.

using structured questionnaire by clinical labs assistants. In addition, qualified nurses collected fasting blood samples using a sterile vacutainer (VACEUTTE® TUBE), needle, and needle holder. All participants' blood samples were stored at room temperature for approximately 45–60 min before being centrifuged at 4000 rpm for 10 min. Following that, aliquots of serum containing at least 1 mL were transferred to labeled Eppendorf tubes for clinical assays. All analyses were performed at the Ibn Al-Haytham Hospital in Amman, Jordan, in a quality-control accredited laboratory.

Total serum 25OHD levels were assayed with chemiluminescent immunoassay technology (DiaSorin, Stillwater, MN, USA), using the DIASORIN LIAISON® 25-hydroxyvitamin D Assay. The assay has a lower limit of detection of around 4 ng/mL. TC, HDL-C, LDL-C, and triglycerides (TG) were quantified in serum using the specific kits M12505i-08, M11523i-26, M11579i-16, and M11528i-20 (BioSystems, Barcelona, Spain). Fasting blood glucose (FBG) levels were analyzed spectrophotometrically using the Cobas C501 analyzer (GLUC3 application; Roche, Mannheim, Germany).

Statistical method

The statistical analyses were performed using the statistical software package SPSS, version 21.0 for Windows (IBM Corporation, Armonk, NY, USA). We calculated frequencies as well as means (SD) of predicted VDD overall for each variable. The *p*-values were considered significant at $p < .05$ and differences between study participants were presented. We calculated Pearson correlations

between 25OHD and each one of the three categories of parameters: lifestyle, anthropometric, and clinical. We used multivariate stepwise regression analysis to identify independent predictors of serum cortisol levels after adjusting for participant characteristics. Normality of distribution for laboratory measurements was tested using the Kolmogorov–Smirnov test and added as a supplementary material (Supplemental Table S1).

Results

Descriptive characteristics

Table 2 summarizes the descriptive and anthropometric characteristics of all participants (n = 270). The mean BMI value corresponds to a simple overweight type (25.09 ± 4.25 kg/m^2). The mean waist circumference (WC) and hip circumference (HC) were 83.11 ± 11.47 cm and 106.19 ± 11.70 cm, respectively. The mean serum 25OHD concentration was 12.34 ng/mL (SD = 6.29 ng/mL) in Table 2, indicating VDD. At baseline, the lipid profile parameters (TG, LDL, HDL, and TC) were recorded for all participants in the study as mentioned in the baseline description of the clinical parameters.

Differences in the levels of lipid profile parameters according to the severity of VDD and independent of CCR (n = 270)

As illustrated in Table 3, a one-way analysis of variance (ANOVA) method was conducted to test whether there were significant differences in lipid profile parameter levels according to the severity of insufficiency of vitamin D (IVD) and irrespective of CCR. One-way ANOVA revealed significant differences in total (TC) scores between various levels of VDD (F = 7.430, $p < .001$). To account for type I error, post hoc multiple comparisons using the Tukey HSD (honestly significant difference) test revealed that the mean scores of TC for the IVD level were significantly different from the mean scores for the other levels (severe vitamin D deficiency (SVD) and deficiency of 25-hydroxyvitamin D (DVD)), which were considered to be indifferent. Significant differences in total (LDL) scores were observed between different levels of VDD (F = 12.910, $p < .001$). Similarly, post hoc multiple comparisons using the Tukey HSD test showed that the mean scores of LDL for the IVD level were substantially different from the mean scores of SVD and DVD, for which they were neutral. There were statistically significant differences in total (non-HDL) cholesterol levels between different levels of VDD (F = 6.137, $p = .002$). Moreover, the Tukey HSD test revealed that the mean non-HDL scores for the IVD level were significantly different from those for the other levels (VD and DVD), for which they were indifferent.

Table 2. Baseline descriptive and anthropometric and lifestyle parameters, (n = 270).

Clinical parameter	Range	Mean ± SD	Normal range
Age (years)	18.0–65.0	27.46 ± 9.87	
Coffee (cups)	0.0–6.0	1.12 ± 1.22	
25OHD (ng/mL)	3.80–29.80	12.34 ± 6.29	30–50
FBG (mg/dL)	54.00–108.00	87.17 ± 10.66	70–110
TC (mg/dL)	131.00–359.00	268.06 ± 37.16	Up to 200
TG (mg/dL)	55.00–271.00	141.45 ± 28.57	Up to 150
HDL (mg/dL)	18.00–95.00	56.28 ± 7.56	≤60
LDL (mg/dL)	54.00–278.00	153.72 ± 21.79	Up to 100
Non_HDL (mg/dL)	76.00–308.00	211.78 ± 36.24	
TC_HDL (mg/dL)	238.18–1561.11	486.27 ± 114.68	
Height (m)	1.40–1.81	1.62 ± 0.06	
BW (kg)	39.00–110.00	66.01 ± 12.04	
BMI (kg/m²)	15.79–43.29	25.09 ± 4.25	
WC (cm)	37.00–130.00	83.11 ± 11.47	
HC (cm)	42.00–153.00	106.19 ± 11.70	
WWR	47.00–179.50	79.86 ± 13.25	
WHR	36.80–166.70	62.40 ± 11.29	

25OHD: 25-hydroxyvitamin D; FBG: fasting blood glucose; TG: triglycerides; TC: total cholesterol; HDL: high-density lipoprotein; LDL: low-density lipoprotein; BMI: body mass index; BW: body weight; WC: waist circumference; HC: hip circumference; WWR: waist circumference ratio; WHR: waist to hip ratio.

Table 3. Differences of selected lipid profile parameters levels based on the severity of VDD and irrespective of coffee consumption rate (n = 270).

Variable	Level	n	Mean ± SD	F	*p*-value
TG	SVD	127	142.24 ± 30.09	0.100	.905
	DVD	104	140.92 ± 27.51		
	IVD	39	140.26 ± 26.86		
	Total	270	141.45 ± 28.57		
HDL	SVD	127	57.28 ± 7.80	2.812	.062
	DVD	104	55.85 ± 7.57		
	IVD	39	54.18 ± 6.28		
	Total	270	56.28 ± 7.56		
TC	SVD	127	272.77 ± 36.13	7.430	.001*
	DVD	104	269.98 ± 35.08		
	IVD	39	247.56 ± 39.96		
	Total	270	268.06 ± 37.16		
LDL	SVD	127	156.97 ± 22.92	12.910	<.001*
	DVD	104	155.63 ± 17.39		
	IVD	39	138.08 ± 22.44		
	Total	270	153.72 ± 21.79		
Non_HDL	SVD	127	215.50 ± 35.50	6.137	.002*
	DVD	104	214.13 ± 34.13		
	IVD	39	193.38 ± 39.40		
	Total	270	211.78 ± 36.24		

TG: triglycerides; TC: total cholesterol; HDL: high-density lipoprotein; LDL: low-density lipoprotein; F statistic: the variation between sample means/variation within the samples; n: number of participants; SVD: severe vitamin D deficiency; DVD: deficiency of vitamin D; IVD: insufficiency of vitamin D.
*indicates statistical significance.

When studying the difference in all variables between the SVD, DVD, and IVD groups, no significant differences were noted for TG and HDL levels. However, the comparison identified significant differences were noted between the SVD, DVD, and IVD groups for TC, LDL, and non-HDL levels ($p > .05$).

Table 4. Differences of 25OHD and lipid profile parameters levels based on the CCR (n = 270).

Dependent Variable	Level	n	Mean ± SD	F	p-value
25OHD	NCC	102	12.52 ± 6.04	1.501	.225
	MCC	134	12.65 ± 6.78		
	HCC	34	10.61 ± 4.65		
	Total	270	12.34 ± 6.29		
TC	MCC	102	273.72 ± 39.73	1.936	.146
	HCC	134	264.92 ± 35.54		
	Heavy	34	263.44 ± 34.27		
	Total	270	268.06 ± 37.16		
TG	NCC	102	146.15 ± 34.87	2.304	.102
	MCC	134	138.19 ± 25.28		
	HCC	34	140.18 ± 15.63		
	Total	270	141.45 ± 28.57		
HDL	NCC	102	57.10 ± 6.83	1.525	.219
	MCC	134	56.09 ± 6.35		
	HCC	34	54.56 ± 12.48		
	Total	270	56.28 ± 7.56		
LDL	NCC	102	152.79 ± 18.33	0.934	.394
	MCC	134	153.22 ± 23.98		
	HCC	34	158.47 ± 22.28		
	Total	270	153.72 ± 21.79		
Non_HDL	NCC	102	216.62 ± 39.12	1.467	.232
	MCC	134	208.83 ± 35.11		
	HCC	34	208.88 ± 30.60		
	Total	270	211.78 ± 36.24		
TC/HDL ratio	NCC	102	483.68 ± 76.75	1.704	.184
	MCC	134	479.74 ± 103.23		
	HCC	34	519.79 ± 211.84		
	Total	270	486.27 ± 114.68		

TG: triglycerides; TC: total cholesterol; HDL: high-density lipoprotein; LD:, low- -density lipoprotein; F statistic: variation between sample means/ variation within the samples; n, number of participants; SVD: severe vitamin D deficiency; DVD: deficiency of vitamin D; IVD: insufficiency of vitamin D; CCR: Coffee consumption rate TG: HCR: heavy coffee consumption rate MCR: moderate coffee consumption rate; NCR; no coffee consumption rate.

Table 3 also shows significant differences in total (TC) scores among different levels of VDD (F = 7.430, p = .001). The post hoc multiple comparisons by the Tukey HSD test indicated that the mean scores of the SVD group were 272.77 ± 36.13 mg/dL, while the TC mean scores for the DVD and IVD groups were 269.98 ± 35.08 mg/dL and 247.56 ± 39.96 mg/dL, respectively. The mentioned scores reflect the effect of VDD on TC, where the severity of deficiency increases.

Differences in 25OHD and lipid profile parameter levels based on the CCR

As described in Table 4, a one-way ANOVA test was conducted to study the significant differences in lipid profile parameter levels based on the CCR. ANOVA showed that there were no significant differences between all item scores among different levels of coffee consumption (NCC, MCC, and HCC).

The correlation of clinical parameters mentioned in the descriptive analysis of the clinical study participants (n = 270) revealed significant positive relationships between coffee drinking and age (r = 0.307, p = .001), coffee drinking and FBG (r = 0.184, p = .05), coffee drinking and the ratio of TC/HDL items (r = 0.134, p = .05), and coffee drinking and body weight (BW) item (r = 0.130, p = .05). In addition, there was a significant negative correlation between coffee drinking and the HDL item (r = −0.161, p < .01), shown in Table 5. This trend was clearer when the study participants were further subdivided by their combined VITD level and coffee consumption behavior into three groups (Table 6).

As presented in Table 6, there was no significant relationship between coffee consumption and other items at the severe deficiency level of VITD, except for the age item, which was significantly more relevant and had a positive direction (r = 0.366, p < .001). Correlation in participants with VDD showed a significant relationship

Table 5. Correlation coefficient between coffee consumption rate and VDD regardless of its severity and lipid.

Clinical Parameter	Correlation coefficient (r)
Age	0.307*
25OHD	−0.084
FBG	0.184*
TC	−0.091
TG	−0.078
HDL	−0.161*
LDL	0.102
Non-HDL	−0.06
TC/HDL ratio	0.134*
BW	0.130*
BMI	0.112
WC	0.097
HC	0.115
WWR	0.082
WHR	0.06

r: correlation coefficient; 25OHD: 25-hydroxyvitamin D; FBG: fasting blood glucose; TG: triglycerides; TC: total cholesterol; HDL: high-density lipoprotein; LDL: low-density lipoprotein; BMI: body mass index; BW: body weight; WC: waist circumference; HC: hip circumference; WWR: waist circumference ratio; WHR: body weight/hip ratio.
*indicates statistical significance.

Table 6. Coefficient correlation between VDD levels with coffee consumption (irrespective of its rate) and lipid profile parameter levels for whole study sample (n = 270).

Clinical parameters	SVD (r)[a]	DVD (r)[b]	IVD (r)[c]
Age (years)	0.102	0.377*	0.366*
FBG (mg/dL)	−0.012	0.323*	0.005
TC (mg/dL)	0.108	−0.137	−0.14
TG (mg/dL)	0.129	−0.096	−0.112
HDL (mg/dL)	0.207	−0.264*	−0.163
LDL (mg/dL)	0.03	0.162	0.03
Non_HDL	0.098	−0.082	−0.107
TC/HDL ratio	0.122	0.246*	0.03
Height(m)	−0.089	0.091	0.084
BW (kg)	−0.086	0.157	0.171
BMI (kg/m²)	−0.045	0.125	0.147
WC (cm)	−0.081	0.143	0.103
HC (cm)	−0.065	0.05	0.174
WWR	−0.008	0.087	0.105
WHR	−0.076	0.127	0.036

r: Pearson correlation coefficient; 25OHD: 25-hydroxyvitamin D; FBG: fasting blood glucose; TG: triglycerides; TC: total cholesterol; HDL: high-density lipoprotein; LDL: low-density lipoprotein; BMI: body mass index; BW: body weight; WC: waist circumference; HC: hip circumference; WWR: waist circumference ratio; WHR: body weight/hip ratio.
[a]Regression coefficient in group with severe VITD deficiency.
[b]Regression coefficient in group with VITD deficiency.
[c]Regression coefficient in group with intermediate VITD deficiency.
(*r) > 0.25.

between coffee consumed and age (r = 0.377, p < .001) and FBG with a Pearson linear correlation coefficient of 0.323 (r = 0.323, p < .01). In addition, TC/HDL was the third

Table 7. Combined versus single association of CCR and VDD with non-HDL and C/HDL ratio in women using two-way ANOVA test.

Association	F-test	p-value
VDD + non-HDL	0.002*	.010*
VDD + TC/HDL	6.579	.002*
CCR + non-HDL	0.448	.639
CCR + TC/HDL	0.813	.445
(Combined CCR + VDD) + non-HDL	1.724	.145
(Combined CCR + VDD) + TC/HDL	4.21	.003*

CCR: coffee consumption rate; VDD: vitamin D deficiency; TC: total cholesterol; HDL: high-density lipoprotein; F: variation between sample means/variation within the samples.
*indicates statistical significance.

item with a significant positive correlation (r = 0.246, p < .05). In contrast, there was a significant negative correlation between coffee consumption and HDL values at the VDD level (r = −0.264, p < .01). At a VITD level of insufficiency, the third group demonstrated that there was no significant relationship between coffee consumed and other things.

As shown in Table 7, a two-way ANOVA was conducted to investigate the effects of CCR, VDD, and their interaction (combined effect) on non-HDL and TC/HDL ratio. Although VDD alone showed a significant effect on both non-HDL and TC/HDL ratios (F-test = 4.680, p = .01; F-test = 6.579, p = .02, respectively), there was no significant effect of the interaction between VDD and CCR on non-HDL. The interaction between the two factors showed only a significant effect on the TC/HDL ratio (F-test = 4.210, p < .05).

Stepwise regression analysis to investigate the effect of VITD on TC/HDL according to different levels of coffee consumption

Stepwise regression analysis was used to determine the predictors of non-HDL at various levels of coffee consumption (Table 8). The multivariate stepwise regression analysis showed that the influence of independent variables (IDVs) on non-HDL-C may explain ~53%, ~66 %, and ~55 % of non-HDL-C values in the NCC, MCC, and HCC groups, respectively. The multiple linear regression models also examined the predictors of the TC/HDL ratio at various coffee levels. The predictors may elucidate 38.7%, 39.1%, and 38.9% of non-HDL-C values in the NCC, MCC, and HCC groups, respectively.

Discussion

The current study demonstrated that VDD alone or in combination with CCR has a positive association with TC/HDL ratio in Jordanian women with VDD. Also, in the same study population and independently of CCR, VDD alone

Table 8. Significant multivariate associations of non-HDL and TC/HDL levels and the study variables selected by stepwise regression based on CCR.

DV	Group	IV	R	R^2	F	B	*p*-value
Non_HDL	NCC	TG	0.661	0.437	77.673	0.625	<.001
		LDL	0.725	0.525	54.808	0.672	<.001
	MCC	TG	0.615	0.378	127.898	0.739	<.001
		LDL	0.813	0.661	80.246	0.904	<.001
	HCC	TG	0.659	0.434	19.159	0.685	<.001
		LDL	0.743	0.553	24.537	0.825	<.001
TC/HDL	NCC	TG	0.467	0.218	27.95	0.338	<.001
		LDL	0.561	0.315	22.727	0.328	<.001
		SME	0.596	0.356	18.022	−0.212	<.001
		Hip	0.622	0.387	15.307	0.338	<.001
	MCC	LDL	0.554	0.307	58.446	2.511	<.001
		Age	0.587	0.344	34.423	1.424	<.001
		TG	0.608	0.37	25.446	0.641	<.001
		VDD	0.625	0.391	20.665	2.28	<.001
	HCC	LDL	0.48	0.23	9.582	5.704	<.001
		VDD	0.624	0.389	9.864	18.949	<.001

CCR: coffee consumption rate TG: HCR: heavy coffee consumption rate; MCR: moderate coffee consumption rate; NCR: no coffee consumption rate; TG: triglycerides; TC: total cholesterol; HDL: high-density lipoprotein; DV: dependent variable; IV: independent variable; R: Pearson correlation coefficient; R^2: regression; F: variation between sample means/variation within the samples; n: number of participants; SVD: severe vitamin D deficiency; DVD: deficiency of vitamin D; IVD: insufficiency of vitamin D.

demonstrated a strong positive correlation with non-HDL levels and TC/HDL ratio. Regardless of which non-HDL or TC/HDL ratio is a more reliable predictor of coronary artery disease (CAD) risk, either alone or in combination with CCR, VDD predicted negative outcomes for both variables. In this context, the negative correlation noted between VDD and non-HDL in the current study is consistent with the results of some prior studies that assessed the atherogenic profile in obese females.[26,33,34] Furthermore, a negative association between the 25OHD level and the risk of CAD, including TG and LDL-C, has been suggested in healthy participants and patients.[33–35] In this respect, it has been demonstrated that people with normal serum 25OHD have a healthier lipid profile than those with VDD.

Nonetheless, as mentioned previously, the association between 25HOD and women's lipid profiles remained unclear. As a result, a U-shaped association between serum 25OHD levels and CVD risk has been proposed to correlate drastic fluctuations in serum 25OHD levels with CVD risk due to its effects on lipid metabolism.[32,36] As a result, the presence or absence of typical risk factors had no effect on the U-shaped relationship.[37]

The TC/HDL ratio has been established as a simple lipid index for predicting CAD risk, and therefore it may be appropriate for the selection of patients with lipid abnormalities who require earlier and more aggressive therapy.[38] Multiple linear regression analyses revealed that TG and LDL were significant IDVs affecting non-HDL and the TC/HDL ratio. A high TG level has been a better predictor of coronary artery disease in women than in men.[39] Low TG (97 mg/dL) and high HDL (>57 mg/dL)

levels are associated with a very low risk of coronary artery disease.[39]

In pregnant and postmenopausal women, as well as among Emirati adult women with type 2 diabetes, low 25OHD levels were also related to an increased risk of dyslipidemia, including a TC/HDL ratio.[8] In addition, based on the regression analysis results in the current study, VDD might be related to a high cholesterol ratio as a provoking factor, which might be related to the CCR.

Regarding the effect of CCR as a risk factor for dyslipidemia, the current study corroborates previous research showing a positive correlation between elevated CCR and TC/HDL ratio. In a study that investigated the relationship between coffee consumption and serum VITD levels in young Koreans, it was discovered that women who consumed the most coffee had the lowest VITD levels.[40] Similarly, a meta-analysis demonstrated that consuming coffee (2.4–8 cups per day) increased TC, LDL, and TG levels after 2 to 11 weeks.[41,42] Finally, another research indicated a weak correlation between moderate coffee consumption and hypercholesterolemia when compared to heavy or very heavy coffee consumption.[43] On the other hand, it was reported that a direct correlation existed between coffee consumption and VITD levels among Saudi Arabian teenagers, irrespective of gender. However, other variables such as diet and coffee type may also affect 25OHD levels.[18] It has been mentioned that the adenosine A2A receptor is a common interaction site for cholesterol as well as for caffeine.[44,45] Many studies have shown that caffeine increases lipolysis and fat oxidation in peripheral tissues after coffee consumption.[46–48] Moreover, caffeine

elevates catecholamine levels, which promotes lipolysis in adipose tissue by stimulating the stress axis sympathetic responses.[49,50]

Caffeine's effect as an adrenoceptor blocker is dose-dependent. For example, propranolol, an adrenoceptor blocker, inhibited caffeine-stimulated energy outflow and lipolysis, indicating that some of caffeine's metabolic effects are mediated by catecholamines.[51] Accordingly, our results are consistent with those of a previous study that revealed that cholesterol elevation by consumption of unfiltered boiled coffee has a dose-dependent effect.[52] Therefore, CCR as well as caffeine dose may explain the inconsistency with the results of a recent study, indicating that caffeine acts to interact in an antagonistic manner to enhance cholesterol metabolism, thereby increasing the expression of the LDL receptors and clearance of LDL.[53]

Regarding the association between CCR and VDD, it has been postulated that caffeine interacts with variants in the vitamin D3 receptor polymorphisms.[18,54,55] It is assumed that the reduction of adipose tissue is accompanied by an increase in serum 25OHD levels.[56] Nevertheless, there is an apparent variation in mean age, which is inversely proportional to body fat mass.[57] Finally, in relation to a potential association between stress and CCR, it has been shown that increasing allostatic stress decreases serum 25OHD levels.[58] However, a number of questions concerning the study design were considered to be a study limitation. First, no data have been recorded concerning the time of coffee consumption and whether the consumption was before, during, or after food intake due to the lack of nutritional data for the participants. Second, based on the records and study design, the CCR has been self-reported by the participant. Third, we did not measure caffeine concentration per cup, which may help us to discuss some inconsistency that has been reported by others.[53]

Conclusion

In conclusion, this study shows that VDD is independently associated with two potential CAD risk factors in women: non-HDL and TC/HDL ratio. VDD and coffee consumption may have a synergistic association in relation to elevated TC/HDL ratio in healthy women. Overall, higher CCR among women with VDD significantly elevated TC/HDL ratio that may increase woman's risk of hyperlipidemia.

Author contribution(s)

Maha Habash: Conceptualization; Data curation; Formal analysis; Writing – original draft.

Sami Al-shakhshir: Data curation; Investigation; Resources.
Mohammad Abusamak: Funding acquisition; Project administration; Resources; Visualization.
Mohammad Yasin Mohammad: Funding acquisition; Investigation; Methodology.
Mahmoud AbuSamak: Data curation; Formal analysis; Funding acquisition; Project administration; Supervision; Validation; Writing – original draft; Writing – review & editing.

ORCID iDs

Maha Habash [iD] https://orcid.org/0000-0003-2152-667X

Mohammad Abusamak [iD] https://orcid.org/0000-0002-7832-1184

Supplemental material

Supplemental material for this article is available online.

References

1. Van Dam RM, Hu FB and Willett WC. Coffee, caffeine, and health. *N Engl J Med* 2020; 383(4): 369–378.
2. Abu-Taha M, Dagash R, Mohammad BA, et al. Combined effect of coffee consumption and cigarette smoking on serum levels of vitamin B12, folic acid, and lipid profile in young male: a cross-sectional study. *Int J Gen Med* 2019; 12: 421–432.
3. Gökcen BB and Şanlier N. Coffee consumption and disease correlations. *Crit Rev Food Sci Nutr* 2019; 59(2): 336–348.
4. Du Y, Lv Y, Zha W, et al. Effect of coffee consumption on dyslipidemia: a meta-analysis of randomized controlled trials. *Nutr Metab Cardiovasc Dis* 2020; 30(12): 2159–2170.
5. Karabudak E, Türközü D and Köksal E. Association between coffee consumption and serum lipid profile. *Exp Ther Med* 2015; 9(5): 1841–1846.
6. Hasoun LZ, Khader HA, Abu-Taha MI, et al. A cross-sectional study on the combined effect of body weight and coffee consumption on serum levels of leptin, vitamin B12, and folic acid in healthy young adult males. *J Multidiscip Healthc* 2021; 14: 639–650.
7. Gebeyehu GM, Feleke DG, Molla MD, et al. Effect of habitual consumption of Ethiopian Arabica coffee on the risk of cardiovascular diseases among non-diabetic healthy adults. *Heliyon* 2020; 6(9): e04886.
8. Shi L, Brunius C, Johansson I, et al. Plasma metabolite biomarkers of boiled and filtered coffee intake and their association with type 2 diabetes risk. *J Intern Med* 2020; 287(4): 405–421.

9. Cai L, Ma D, Zhang Y, et al. The effect of coffee consumption on serum lipids: a meta-analysis of randomized controlled trials. *Eur J Clin Nutr* 2012; 66(8): 872–877.

10. Bergmann K. Non-HDL cholesterol and evaluation of cardiovascular disease risk. *EJIFCC* 2010; 21(3): 64–67.

11. Blaha MJ, Blumenthal RS, Brinton EA, et al. The importance of non-HDL cholesterol reporting in lipid management. *J Clin Lipidol* 2008; 2(4): 267–273.

12. Dong J, Yang S, Zhuang Q, et al. The associations of lipid profiles with cardiovascular diseases and death in a 10-year prospective cohort study. *Front Cardiovasc Med* 2021; 8: 745539.

13. Jee SH, He J, Appel LJ, et al. Coffee consumption and serum lipids: a meta-analysis of randomized controlled clinical trials. *Am J Epidemiol* 2001; 153(4): 353–362.

14. Pandeya A, Sharma M, Regmi P, et al. Pattern of dyslipidemia and evaluation of non-HDL cholesterol as a marker of risk factor for cardiovascular disease in type 2 diabetes mellitus. *Nepal Med Coll J* 2012; 14(4): 278–282.

15. Cheung RJ, Gupta EK and Ito MK. Acute coffee ingestion does not affect LDL cholesterol level. *Ann Pharmacother* 2005; 39(7–8): 1209–1213.

16. Zargar A, Auttapibarn C, Hong SH, et al. The effect of acute café latte ingestion on fasting serum lipid levels in healthy individuals. *J Clin Lipidol* 2013; 7(2): 165–168.

17. Abu-Samak MS, AbuRuz ME, Masa'Deh R, et al. Correlation of selected stress associated factors with vitamin D deficiency in Jordanian men and women. *Int J Gen Med* 2019; 12: 225–233.

18. Al-Othman A, Almusharaf S, Al-Daghri N, et al. Tea and coffee consumption in relation to vitamin D and calcium levels in Saudi adolescents. *Nutr J* 2012; 11: 56.

19. Al-Dujaili EAS, Munir N and Iniesta RR. Effect of vitamin D supplementation on cardiovascular disease risk factors and exercise performance in healthy participants: a randomized placebo-controlled preliminary study. *Ther Adv Endocrinol Metab* 2016; 7(4): 153–165.

20. Abdelbaset-Ismail A, Pedziwiatr D, Suszyńska E, et al. Vitamin D3 stimulates embryonic stem cells but inhibits migration and growth of ovarian cancer and teratocarcinoma cell lines. *J Ovarian Res* 2016; 9(1): 26.

21. Nakamura K, Kitamura K, Takachi R, et al. Impact of demographic, environmental, and lifestyle factors on vitamin D sufficiency in 9084 Japanese adults. *Bone* 2015; 74: 10–17.

22. Rerksuppaphol L and Rerksuppaphol S. Comparison of equations for the calculation of low-density lipoprotein cholesterol in Thai population. *J Nat Sci Biol Med* 2021; 12: 224.

23. Subber Z, Hashim H and Al-Shamma G. The impact of vitamin D level on serum lipids in type 2 diabetes mellitus. *Baghdad J Biochem Appl Biol Sci* 2021; 2(04): 230–236.

24. Khan W, Augustine D, Rao RS, et al. Lipid metabolism in cancer: a systematic review. *J Carcinog* 2021; 20(1): 4.

25. Nakhl S, Sleilaty G, El Samad S, et al. Association between vitamin D deficiency and lipid and non-lipid markers of cardiovascular diseases in the middle east region. *Eur J Clin Nutr* 2019; 73(6): 850–858.

26. Curvello-Silva KL, Oliveira NA, Silva TSS, et al. Association between cardiovascular risk factors and 25(OH) D levels in obese patients. *Metab Syndr Relat Disord* 2020; 18(7): 328–332.

27. Schwetz V, Scharnagl H, Trummer C, et al. Vitamin D supplementation and lipoprotein metabolism: a randomized controlled trial. *J Clin Lipidol* 2018; 12(3): 588.e4–596.e4.

28. Buckley AJ, Barakat MT, Holick MF, et al. Parameters of bone and cardiovascular health related to 25-hydroxyvitamin D status in Emirati nationals attending primary care and diabetes services: a retrospective cohort study. *Sci Rep* 2019; 9(1): 3835.

29. Dibaba DT. Effect of vitamin D supplementation on serum lipid profiles: a systematic review and meta-analysis. *Nutr Rev* 2019; 77(12): 890–902.

30. Akbari M, Moosazaheh M, Lankarani KB, et al. The effects of vitamin D supplementation on glucose metabolism and lipid profiles in patients with gestational diabetes: a systematic review and meta-analysis of randomized controlled trials. *Horm Metab Res* 2017; 49(9): 647–653.

31. Manson JE, Cook NR, Lee IM, et al. Vitamin D supplements and prevention of cancer and cardiovascular disease. *N Engl J Med* 2018; 380(1): 33–44.

32. Church DD, Hoffman JR, LaMonica MB, et al. The effect of an acute ingestion of Turkish coffee on reaction time and time trial performance. *J Int Soc Sports Nutr* 2015; 12: 37.

33. Tamer G, Telci Caklili O, Gungor K, et al. Effect of vitamin D status on lipid profile in premenopausal women: a cross-sectional study. *Cardiovasc Endocrinol* 2017; 6(2): 86–91.

34. Tabrizi R, Hallajzadeh J, Mirhosseini N, et al. The effects of vitamin D supplementation on muscle function among postmenopausal women: a systematic review and meta-analysis of randomized controlled trials. *EXCLI J* 2019; 18: 591–603.

35. Adikaram SGS, Samaranayake DBDL, Atapattu N, et al. Prevalence of vitamin D deficiency and its association with metabolic derangements among children with obesity. *BMC Pediatr* 2019; 19(1): 186.

36. Lupton JR, Faridi KF, Martin SS, et al. Deficient serum 25-hydroxyvitamin D is associated with an atherogenic lipid profile: the Very Large Database of Lipids (VLDL-3) study. *J Clin Lipidol* 2016; 10(1): 72.e1–81.e1.

37. Dror Y, Giveon SM, Hoshen M, et al. Vitamin D levels for preventing acute coronary syndrome and mortality: evidence of a nonlinear association. *J Clin Endocrinol Metab* 2013; 98(5): 2160–2167.

38. Boizel R, Benhamou P, Lardy B, et al. Ratio of triglycerides to HDL cholesterol an indicator of LDL particle size in patients with type 2 diabetes and normal HDL cholesterol levels. *Diabetes Care* 2000; 23: 1679–1685.

39. Pathak LA, Shirodkar S, Ruparelia R, et al. Coronary artery disease in women. *Indian Heart J* 2017; 69(4): 532–538.

40. Lim HS, Lee HH, Byun DW, et al. Serum vitamin D level related to coffee consumption in Korean young adults using the 5th Korea national health and nutrition examination survey. *J Bone Metab* 2017; 24(4): 229–233.

41. Farias-Pereira R, Park CS and Park Y. Mechanisms of action of coffee bioactive components on lipid metabolism. *Food Sci Biotechnol* 2019; 28(5): 1287–1296.

42. Grosso G, Godos J, Galvano F, et al. Coffee, caffeine, and health outcomes: an umbrella review. *Annu Rev Nutr* 2017; 37: 131–156.

43. Panagiotakos DB, Pitsavos C, Chrysohoou C, et al. The J-shaped effect of coffee consumption on the risk of developing acute coronary syndromes: the CARDIO2000 case-control study. *J Nutr* 2003; 133(10): 3228–3232.

44. Rouviere E, Arnarez C, Yang L, et al. Identification of two new cholesterol interaction sites on the A(2A) adenosine receptor. *Biophys J* 2017; 113(11): 2415–2424.

45. Doré AS, Robertson N, Errey JC, et al. Structure of the adenosine A(2A) receptor in complex with ZM241385 and the xanthines XAC and caffeine. *Structure* 2011; 19(9): 1283–1293.

46. McGraw C and Robinson AS. Membrane cholesterol and the adenosine A2a receptor. *Biophys J* 2017; 112(3): 33a–34a.

47. Flanagan J, Bily A, Rolland Y, et al. Lipolytic activity of Svetol®, a decaffeinated green coffee bean extract. *Phytother Res* 2014; 28(6): 946–948.

48. Vandenberghe C, St-Pierre V, Courchesne-Loyer A, et al. Caffeine intake increases plasma ketones: an acute metabolic study in humans. *Can J Physiol Pharmacol* 2017; 95(4): 455–458.

49. Carrageta DF, Dias TR, Alves MG, et al. Anti-obesity potential of natural methylxanthines. *J Funct Foods* 2018; 43: 84–94.

50. Kogure A, Sakane N, Takakura Y, et al. Effects of caffeine on the uncoupling protein family in obese yellow KK mice. *Clin Exp Pharmacol Physiol* 2002; 29(5–6): 391–394.

51. Wu L, Meng J, Shen Q, et al. Caffeine inhibits hypothalamic A(1)R to excite oxytocin neuron and ameliorate dietary obesity in mice. *Nat Commun* 2017; 8: 15904.

52. Aro A, Teirilä J and Gref CG. Dose-dependent effect on serum cholesterol and apoprotein B concentrations by consumption of boiled, non-filtered coffee. *Atherosclerosis* 1990; 83(2–3): 257–261.

53. Lebeau PF, Byun JH, Platko K, et al. Caffeine blocks SREBP2-induced hepatic PCSK9 expression to enhance LDLR-mediated cholesterol clearance. *Nat Commun* 2022; 913(1): 770.

54. Bennett JM, Fagundes CP and Kiecolt-Glaser JK. The chronic stress of caregiving accelerates the natural aging of the immune system. In: Bosch J, Phillips A and Lord J (eds) *Immunosenescence*. New York: Springer, 2013, pp. 35–46.

55. Rapuri PB, Gallagher JC, Kinyamu HK, et al. Caffeine intake increases the rate of bone loss in elderly women and interacts with vitamin D receptor genotypes. *Am J Clin Nutr* 2001; 74(5): 694–700.

56. Sergeev IN. Vitamin D status and vitamin D-dependent apoptosis in obesity. *Nutrients* 2020; 12(5): 1392.

57. Mott JW, Wang J, Thornton JC, et al. Relation between body fat and age in 4 ethnic groups. *Am J Clin Nutr* 1999; 69(5): 1007–1013.

58. Frei R, Haile SR, Mutsch M, et al. Relationship of serum vitamin D concentrations and allostatic load as a measure of cumulative biological risk among the US population: a cross-sectional study. *PLoS ONE* 2015; 10(10): e0139217.