The relation of serum vitamins C and E levels and the severity of angiographically defined coronary artery disease in Alsader Teaching Hospital in Basrah

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ABSTRACT

***Objective*: To assess the relationship between the serum concentrations of vitamins C & E and the severity of coronary artery disease.**

***Subjects and methods*: In a case-control study, we evaluated 200 patients who underwent coronary angiography at AL-Basrah Cardiac Center at Al-Sader Teaching Hospital, Basra, Iraq. They were separated into two groups of case (patients with CAD) and control (non CAD). Four milliliters of blood samples were taken for measuring vitamin E and C. For statistical analyses, chi-square test, Student's t-test, one-way ANOVA, and the logistic regression were used.**

***Results*: In the present study, 94 participants with CAD in the case group and 106 participants free of CAD in the control group were included in the analysis. At baseline, there were significant differences in serum vitamin C ,vitamin E and some cardiovascular risk factors(diabetes, hypertension and smoking habits) between the two groups ($P < 0.05$). Moreover, when other risk factors of CVD were included in the model, serum vitamin C (Odd Ratio (OR = 0.8, 95% CI= 0.68-0.92, P = 0.0001) and serum Vitamin E (OR = 0.66, 95% CI = 0.578-0.754, P = 0.0001) were associated with CAD. There were a significant ($P < 0.05$) statistical changes in the vitamin C and E among the three sub groups of CAD patients being more deficient as the disease become more severe.**

***Conclusions*: Low serum vitamin C and E concentrations were associated with CAD and related to its severity.**

***Key words*: Vitamin C, vitamin E, Coronary Artery Disease, Coronary Angiography.**

تقييم العلاقة بين مستوى فيتامين هـ وفيتامين ج وشدة مرض الشرايين التاجية المثبت قسطارياً في مستشفى الصدر التعليمي في البصرة.

الهدف من الدراسة: تقييم مستوى فيتامين ج وفيتامين هـ عند مرضى الشريان التاجي وعلاقتها بشدة المرض.

طريقة اجراء الدراسة: صممت الدراسة الحالية على شكل دراسة لحالة مراقبة ، قد تم العمل في كلية طب البصرة قسم الكيمياء الحياتية. تضمنت مجموعة الدراسة ٩٤ من المرضى ذكورا واناثا والذي تتراوح اعمارهم من ٣٥-٨٥ سنة الذين يراجعون مركز البصرة لطب وجراحة القلب في مستشفى الصدر التعليمي، والذين اظهرت نتائج قسطرة الشرايين التاجية وجود اكثر من ٥٠% تضييق في واحد او اثنين او ثلاث من شرايين القلب التاجية. شملت المجموعة الضابطة ١٠٦ مرضى (من الذين يرجعون نفس المركز) ذكورا واناثا والذي تتراوح اعمارهم من ٢٩-٨٠ سنة و المطابقة لمجموعة الدراسة في العمر والجنس والطول والوزن والذين اظهرت نتائج قسطرة الشرايين القلبية خلو الشرايين من اي تضييق. قسمت مجموعة المرضى الى ثلاثة مجاميع (الذين لديهم شريان واحد متضيق او شريانين او ثلاث شرايين). جمعت عينات من الدم (٤ مل) باستخدام سرنجة معقمة من كلا المجموعتين. تم فصل وتجميع مصل الدم لغرض قياس كل من فيتامين ج و فيتامين هـ.

نتائج الدراسة: اظهرت نتائج الدراسة وجود نقصان معنوي ($P < 0.05$) في مستوى فيتامين ج، فيتامين هـ في مرضى الشريان التاجي مقارنة بالمجموعة الضابطة. كما اظهرت الدراسة الحالية ايضا ان هناك علاقة سلبية معنوية ($P < 0.05$) بين فيتامين ج، فيتامين هـ و شدة المرض.

استنتاجات الدراسة: ان نقصان الفيتامينات (ج وهـ) لهم دور مهم للإصابة بمرض الشريان التاجي وكلما قل تركيزهما بالدم زادت شدة المرض.

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INTRODUCTION

Coronary Artery Disease (CAD) is the chief cause of mortality and morbidity in most countries.[1] Traditional risk factors for CAD development including hypertension, hyperlipidemia, diabetes mellitus, age, sex, obesity, positive family history and cigarette smoking,[2] the oxidative stress and inflammation are being considered as recent and significant risk factors.[3-5] The principal cause of CAD is atherosclerosis[6] which is a chronic immunoinflammatory, fibroproliferative disease of large and medium-sized arteries fuelled by lipid. Endothelial cells, leukocytes, and intimal smooth muscle cells are the key players in the development of CAD.[7-9] According to the theory of oxidative stress, atherosclerosis is the result of the oxidative modification of low density lipoproteins (LDL) in the arterial wall by reactive oxygen species (ROS). Evidence suggests that traditional risk factors for atherosclerosis increase the risk of the production of free ROS, not only from the endothelial cells, but also from the smooth muscle cells and the adventitial cells.[10] Vitamin E is an antioxidant that acts as a scavenger for molecular oxygen and free radicals,[11] the major biologic role of tocopherol is to protect polyunsaturated fatty acids (PUFAs) and other components of cell membranes and LDL from oxidation by free radicals. It is mostly effective in avoiding lipid peroxidation.[12,13] Both *in vitro* and *in vivo* studies have established that α-tocopherol inhibits LDL oxidation and decreases the release of reactive oxygen species.[14] As an antioxidant, vitamin C chief role is to neutralize free radicals. Since ascorbic acid is water soluble, it can work both inside and outside the cells to defeat free radical damages. Free radicals look for an electron pair to regain their stability. Vitamin C is a good source of electrons so it can donate electrons to free radicals such as hydroxyl and superoxide radicals and quench their reactivity.[15] Vitamin C has a maintaining effect on vitamin E so that it is reduced by vitamin C after neutralizing the radicals by vitamin E. Therefore, it increases the potential of vitamin E in a biologic environment. Vitamin C is the leading defense system against oxidative stress.[13] To further investigate the hypothesis of a link between the oxidative stress and cardiovascular disease we analyze the serum levels of vitamin C, E, as an indicator of antioxidant system in CAD patients and comparing the differences of serum vitamins concentrations according to the number of diseased vessels as criterion for the severity of the disease.

SUBJECTS AND METHODS

This study was conducted as case control and worked at Basra Medical College in Department of Biochemistry on ninety four patients (who attended AL-Basra Cardiac Center at Al-Sader Teaching Hospital, seeking for coronary angiography) with age ranged from 37 to 86 years old in whom coronary angiography revealed that they have > 50% stenosis in one or more coronary arteries. One hundred and six patients from the same center their age range from 29 to 80 years old consider to be a control group with a normal coronary angiogram. Coronary artery disease patients were divided into three groups (single vessel disease, two vessel disease and three vessel disease) according to the number of their obstructed coronary arteries as a marker for the disease severity.[16] The medical history and the results of angiograms were taken through special questionnaire. Approximately four milliliters of venous blood samples were obtained from both control individuals and patients with CAD. The separated serum were used for the assessment of serum vitamin C by Colorimetric method, vitamin E by ELISA kit, causabio, China. Statistical analyses was done by chi-square test, Student's t-test, one-way ANOVA test, and the logistic regression.

RESULTS

(Table-1), shows that the study population composed from 94 Angiographically documented CAD patients most of them in their sixth and seventh decade of life (mean age (59.25±10.73) years), 71.2% of them are males, compared with 106 of CAD free patients and there is no statistical difference between them and CAD patients (P > 0.05) in terms of age, sex, weight, height, BMI, family history of both diabetes and hypertension.

Table 1. Demographic and clinical characteristics of the study population

Variables		CAD N=94	NON CAD N=106
Age (years) means ± SD		59.25 ± 10.73	57.21 ± 10.63
Sex n(%)	Male	67(71.2)	74(69.8)
	Female	27(28.7)	32(30.2)
Weight(kg) mean ± SD		77.09 ± 10.66	75.72±9.35
Height(m) mean ± SD		1.60 ± 0.06	1.62±0.08
BMI (kg/m^2) mean ± SD		29.84 ± 4.10	28.94±4.09
Systolic blood pressure mean ± SD		154 ± 20.0	140±8.0*
Diastolic blood pressure mean ± SD		85 ± 15	80±10*
Family history n(%)	Diabetes mellitus	40(42.5)	34(32.1)
	Hypertension	39(41.4)	46(43.4)
Diabetes mellitus n(%)		51(54.2)	22(20.8)*
Hypertension n(%)		56(59.5)	37(34.9)*
Physical activity Status n(%)	Active	12(12.7)	14(13.2)
	Inactive	82(87.2)	92(86.8)
Smoking status n(%)	Current Smoker	30(31.9)	19(17.9)*
	Non smoker	64(68)	87(82.1)*

*** P-value < 0.05 and consider statistically significant.**

Both groups have sedentary life style and there was a significant statistical difference in smoking behavior between them (P-value < 0.05) with CAD patients being more smoker than the contrary group. There is a significant higher prevalence of diabetes mellitus and hypertension in patients than control group (P-value < 0.05). The differences in systolic and diastolic blood pressure was statically significant (P-value < 0.05) being high in patients group.

Table 2. Drug administration in the study population

Name of the drug	CAD*N=94	Non CAD N=106
Statin	68(72.3)	52(49.05)
B blocker	47(50)	29(27.35)
Aspirin	82(87.2)	45(42.45)
OHD	51(54.2)	20(18.86)
Clopidogrel	86(91.4)	33(31.13)

***Values expressed by n(%).**

Both groups on different types of drug mostly taken aspirin, statins, oral hypoglycemic drugs, beta blocker and clopidogrel as shown in (**Table-2).** In the patients group 42.55% of them had one blood vessel occluded while the rest had two and three stenosed blood vessel (29.79%, 27.66) respectively as they were illustrated in (**Table-3)**.

Table 3. Classification of coronary artery disease patients according to the number of diseased blood vessel

Number of blood vessel diseased	Number	%
Single vessel	40	42.55
Two vessels	28	29.79
Three vessels	26	27.66
Total	94	100

From (**Table-4)**, it is clearly shown that the serum levels of vitamin C and E level ware significantly (P-value < 0.05) lower in CAD patients than non CAD ones.

Table 4. Biochemical parameters in the study population.

*Parameters	CAD N=94	Non CAD N=106	P value**
Vitamin C (mg/dl)	0.51 ± 0.17	1.64 ± 0.58	0.0001
Vitamin E(µmol/L)	7.62 ± 1.61	10.17 ± 2.16	0.0001

***Values expressed as mean ± SD**

**** P-value < 0.05 consider statistically significant.**

In logistic regression analysis, serum vitamin C and E ware significantly associated with CAD (OR = 0.8, 95% CI = 0.68-0.92, P = 0.0001) and (OR = 0.66, 95% CI = 0.578-0.754, P = 0.0001) respectively after adjustment for traditional risk factors in the study population (**Table-5**), while no such association was found regarding the other factors.

Table 5. Logistic regression analysis adjusting for all major cardiovascular risk factors

Parameters	Case (n=94)	Control (n=106)	OR	95% CI		*P-value
				Lower limit	Upper limit	
Vitamin C^	0.51 ± 0.17	1.64 ± 0.58	0.800	0.68	0.92	0.0001
Vitamin E^	7.62 ± 1.61	10.17 ± 2.1	0.660	0.578	0.754	0.0001
Age^	59.25 ± 10.73	57.21 ± 10.63	1.080	0.85	1.31	0.870
Sex: # *Male*	67(71.2)	74(69.8)	1.12	0.74	1.5	0.670
Female	27(28.7)	32(30.2)	2.04	0.65	3.43	0.480
BMI^	29.84±4.1	28.94 ± 4.09	1.61	0.65	2.57	0.640
Family hx. Of DM#	40(42.5)	34(32.1)	1.09	0.88	1.3	0.345
Family hx. of HT#	39(41.4)	46(43.4)	1.18	0.73	1.63	0.176
DM#	51(54.2)	22(20.8)	3.50	0.98	6.02	0.061
HT#	56(59.5)	37(34.9)	3.04	0.92	5.16	0.060
Smoking#	30(31.9)	19(17.9)	4.03	0.87	7.19	0.063

*** P value < 0.05 consider statistically significant. ^ values expressed as mean ± SD. # value express as n(%).**

It is clear that serum level of vitamin C and E showed a highly significant difference (P-value < 0.05) between the three blood vessel being highest in single vessel and lowest in triple vessel disease as shown in (**Table-6).**

Table 6. Comparison of the patient's antioxidant vitamins (C and E) and the number of diseased blood vessels.

**Vitamins	One vessel	Two vessels	Three vessels	*P-value
Vitamin C	0.64±0.07	0.51±0.11	0.31±0.13	0.001
Vitamin E	8.93±1.51	7.14±0.75	6.13±0.46	0.001

***P < 0.05 consider statistically significant**

****Values expressed as mean ± SD**

DISCUSSION

The CAD patients and control were matched in terms of age, sex, weight, height, BMI, family history of both diabetes and hypertension. Both of them are physically in active (**Table-1**). From the data collected in this study, The history of diabetes, hypertension and smoking were significantly differed between CAD and non CAD patients, being more in patients group, this finding was close to other study done by Alissa et al[17] while differ from a study done by Cebi et al.[18] This high prevalence of traditional risk factor ensure their role in the developments of CAD. Serum vitamins E and C remain statically significant after adjustment for other risk factors with logistic regression (**Table-5**). The current study demonstrated significantly a lower serum level of α- tocopherol among CAD patients than the control group (**Table-4**), which agreed with other studies.[18-21] However, other researchers (Frki, et al (2000)[22] and (Tavallaie, et al (2012)[23] found that there was no statistical difference in the level of vitamin E between CAD and non CAD patients. This low vitamin E could be due to over consumption of antioxidants or low dietary intake. Our results emphasize a negative relation between vitamin E level and the number of stenosed coronary arteries (**Table-6**). This result in agreement with study on Iranian population[20] while similar to study were done in Turkey.[19] This finding ensure the antioxidant role of vitamin E in atherosclerosis. The current study revealed a highly significant decrease in the serum level of ascorbic acid in CAD positive patients as compared with CAD negative patients (**Table-4**), this results also consistent with that of other studies[19,20,24] while inconsistent with other.[25] The possible causes behind low vitamin C maybe due to over consumption as antioxidants, over used in regeneration of vitamin E also may be due to low dietary intake. Vitamin C had negatively correlated with the severity of the disease as shown in (**Table-6)** this result was agreed with other reports,[19,26] this meaningful result revealed that as vitamin C become low the oxidative stress become worse and the disease become more severe.

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