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The Association of CRP and Vitamin D Deficiency with Cardiovascular Disease: A Study among Prediabetic Patients in Andijan City and Markhamat District of the Republic of Uzbekistan

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Abstract The study aimed to assess the association between C-reactive protein (CRP), vitamin D deficiency, and cardiovascular diseases in patients with prediabetes in Andijan city and Markhamat district, Uzbekistan. A total of 3,400 individuals at risk were examined using the Findrisk questionnaire and laboratory tests. Results showed significantly elevated levels of CRP, uric acid, and plasma renin in prediabetic patients compared to the control group ($p<0.005$; $p<0.0001$). An inverse correlation was found between vitamin D levels and CRP, renin, and uric acid, indicating their potential role in cardiovascular risk among prediabetic individuals.

Keywords Vitamin D, C-reactive protein, Prediabetes

1. Introduction

Cardiovascular disease (CVD) is commonly perceived as a major public health problem leading to high morbidity and mortality rates. Extensive and mounting evidence suggests that inflammation is an important part of this chronic condition [1]. Vitamin D is a fat-soluble steroid that has been found to play an important role in the regulation of inflammatory cytokines and immune cells [2]. Novel studies have shown that vitamin D deficiency is associated with increased inflammatory responses and immune system activation, and may have an inverse relationship with various pathological processes such as myocardial infarction [3,4,5].

C-reactive protein (CRP), which is a sensitive indicator of inflammation, has been demonstrated as an important element in predicting cardiovascular disease in a number of prospective epidemiological studies. One such study suggested that the inclusion of SRB measurement in screening based on lipid levels could significantly improve the methodology for identifying women at risk of cardiovascular events [6,7,8].

Observational studies have demonstrated an association between reduced serum vitamin D levels and an increased risk of cardiovascular disease. At the same time, optimal vitamin D levels seem to have a positive effect on the cardiovascular system, which may be partly explained by its immunomodulatory and anti-inflammatory properties [9,10,11].

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Randomised controlled trials (RCTs) and information on the relationship between vitamin D intake through food or supplements and cardiovascular disease risk show mixed results: some studies indicate a beneficial effect, while others find no association with cardiovascular disease. There is a possibility that the effect of vitamin D supplementation may vary depending on C-reactive protein (CRP) levels [12].

All of the above provided the basis for the present study.

The aim of the study was to investigate the association of C-reactive protein and vitamin D deficiency with cardiovascular diseases: a study among patients with prediabetes in Andijan city and Markhamat district of the Republic of Uzbekistan.

2. Material and Methods of Research

The study was conducted on the basis of Andijan State Medical Institute. In total 3400 persons of risk groups were examined, of which 1800 were residents of Markhamat district of Andijan region and 1600 residents of Andijan city. The control group consisted of 30 healthy people.

Inclusion criteria: individuals over 20 years of age who were overweight, dyslipidaemic or hypertensive.

Exclusion criteria: type 1 diabetes mellitus, other endocrine diseases, metformin use, severe autoimmune diseases, vasculitis, oncology.

According to the design, the study was conducted in two phases.

At stage 1, according to the study design, cardiovascular

risk factors including waist circumference, body mass index (BMI), blood pressure level, lipid profile, presence of diabetes mellitus and metabolic syndrome, and anamnestic information extracted from relevant medical records were analysed. Patients were questionnaired using the Findrisk scale.

At the 2nd stage, freshly collected biological material (venous blood) was collected and then promptly delivered to the laboratory for research.

The study methods included general clinical approaches, biochemical testing (measurement of fasting blood glucose levels and two hours after meals, determination of glycated haemoglobin, bilirubin (both direct and indirect), as well as ALT, AST, PTI, coagulogram, C-reactive protein, urea, creatinine and lipid profile), hormonal analyses (insulin and C-peptide levels in the blood as needed) and instrumental methods such as ECG, ultrasound of endocrine glands and internal organs, chest X-ray and other tests.

Data were expressed as mean ± SD, n (%) or OR (95% CI), all statistical tests were two-sided, and a P value < 0.05 was considered statistically significant.

Multiple logistic regression was used to determine the independent association between 25(OH)D status, with normal 25(OH)D as the reference category, and high and low CRP and CVD levels, respectively, after adjusting for demographic variables including age, sex, physical activity, education level, marital status, family history, chronic kidney disease, alcohol consumption, BMI, hypertension, diabetes mellitus, and hypercholesterolemia.

We selected covariates as potential confounders based on previous studies or on their biological plausibility. The following covariates were included in our association analysis: age, sex, body mass index (BMI), marital status, education level, smoking status, alcohol consumption, physical activity, hypertension, diabetes, hypercholesterolaemia, chronic kidney disease (CKD), BMI, and dyslipidaemia.

3. Results of the Study

Figure 1 shows the material and design of the study.

The next step of our research was to assess the content of vitamin D and C-reactive protein in the study groups by region. These data are shown in Table 1.

The data in Table 1 show that the mean values of CRP were significantly higher than the control group in all groups and regions ($p<0.005$; $p<0.0001$). At the same time, mean values of uric acid vitamin were significantly higher in patients in all groups ($p<0.005$). Also, mean plasma renin values were significantly elevated in all patient groups ($p<0.005$; $p<0.0001$).

Further we studied the prevalence of vitamin D3 deficiency in prediabetics in comparative aspect in Markhamat district and Andijan city (Table 2 and 3).

Table 2 shows that a total of 132 (71.7%) patients with various degrees of vitamin D deficiency were identified among 184 patients in Markhamat district. That is, the predominant majority had vitamin D deficiency, with 24 (13%) having severe deficiency, 66 (35.8%) having moderate deficiency, 27 (14.7%) having moderate deficiency and 15 (8.2%) having mild deficiency.

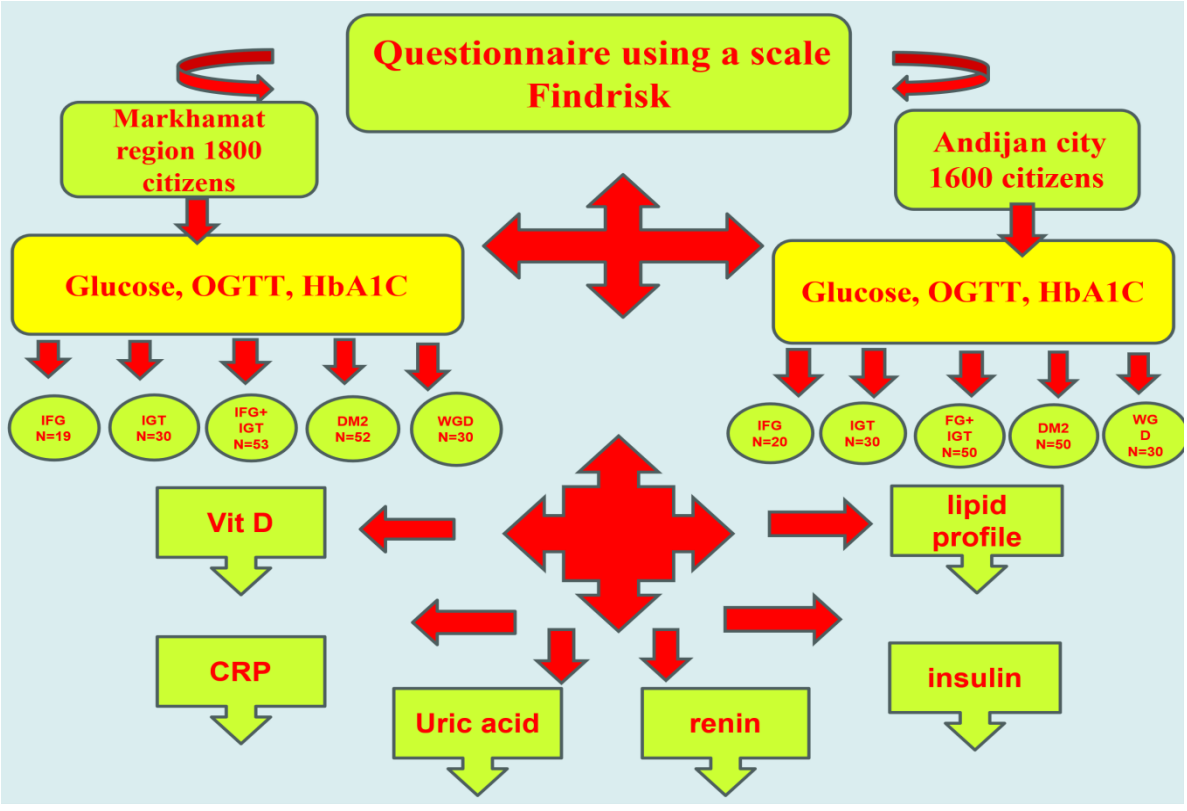

Figure 1. Material and study design

Table 3 shows that a total of 129 (71.6%) patients with different degrees of vitamin D deficiency were identified among 180 patients in Andijan city. That is, the predominant majority had vitamin D deficiency, with 9 (5.0%) having severe deficiency, 92 (51.1%) having moderate deficiency, 25 (13.9%) having moderate deficiency and 3 (1.6%) having mild deficiency.

Thus, we see that vitamin D deficiency of severe degree dominated in Markhamat district - 24 cases: 9 cases in Andijan city.

The last step was the correlation analysis between vitamin D deficiency as a leading risk factor for CVD with renin, CRP and other parameters (Table 4).

Table 1. Mean value of laboratory vitamin D and C-reactive protein in the study groups by region

groups		C-reactive protein, mg/litre	Uric acid, µmol/l	Renin,
IFG	Marhamat	9,8±0,41**	297,5±10,6*	182,5±12,0**
	City	10,4±0,38**	293,0±11,1*	204,7±13,5 **
IGT	Marhamat	9,6±0,40**	333,4±10,5*	180,2±9,7**
	City	9,2±0,41**	321,8±11,4*	185,9±9,1**
IFG +IGT	Marhamat	9,3±0,42**	287,3±10,5*	202,8±12,5 **
	City	10,2±0,45**	319,5±12,5*	205,8±9,0 **
NCMD	Marhamat	5,4±1,31*	223,0±12,3*	77,6±10*
	City	5,1±1,87*	271,3±3,5*	66,0±5,0*
Control		2,5±0,34*	203, 4±6,8	23.2 ±3,2

Note: IFG - impaired fasting glycemia, IGT - impaired glucose tolerance, DM 2 - type 2 diabetes mellitus,
NCMD - no carbohydrate metabolism disorders
Note: * - reliability of differences "p" in comparison with control indices *-P<0.005; **-P<0.0001)

Table 2. Prevalence of vitamin D3 deficiency in prediabetics in Markhamat district

		Normal more than 30 nmol/l		Insufficiency 20-30 nmol/l.		10-20 nmol/L deficiency		Severe deficiency less than 10 nmol/L	
		abs.	%	abs.	%	abs.	%	abs.	%
IFG n=19	commonly.	-	-	4	21,1	10	52,6	5	26,3
IGT, n=30	commonly.	1	3,3	6	20,0	16	53,3	7	23,3
IFG +IGT, n=53	commonly.	-	-	7	13,2	35	66,0	11	20,8
NCMD, n=30	commonly.	14	46,7	10	33,3	5	16,7	1	3,3
Total		15	8.2	27	14.7	66	35.8	24	13.0

Table 3. Prevalence of vitamin D3 deficiency in prediabetics in Andijan

CITY		Normal more than 30 nmol/l		Insufficiency 20-30 nmol/l.		10-20 nmol/L deficiency		Severe deficiency less than 10 nmol/L	
		abs.	%	abs.	%	abs.	%	abs.	%
IFG, n=20	commonly.	-	-	1	5,0	15	75,0	4	20,0
IGT, n=30	commonly.	-	-	6	20,0	23	76,7	1	3,3
IFG +IGT, n=50	commonly.	1	2,0	5	10,0	40	80,0	4	8,0
NCMD, n=30	commonly.	2	6,7	13	43,3	14	46,7	-	-
Total		3	1.6	25	13.9	92	51.1	9	5.0

Table 4. Correlation between vitamin D deficiency as a leading CVD risk factor with renin, CRP and uric acid in prediabetic patients in Markhamat district and Andijan city

Indicators	Vitamin D							
	IFG		IGT		NGN+IGT		NCMD	
	Marhamat	City	Marhamat	City	Marhamat	City	Marhamat	City
Renin	-0,40*	-0,49*	-0,44*	-0,40*	-0,43*	-0,45*	0,01	0,06
C-reactive protein	-0,44*	-0,59*	-0,42*	-0,46*	-0,36	-0,47*	0,11	0,07
Uric acid	-0,47*	-0,48*	-0,41*	-0,35	-0,43*	-0,38	0,25	-0,04

Note: * - reliability of differences "p" in comparison with control indices (*-P<0.005; **-P<0.0001)

Table 4 shows that there was a significant inverse correlation between vitamin D, CRP, renin and uric acid content in almost all groups of prediabetic patients from both regions ($p<0.005$).

Thus, in this study we analysed the hypothesis of the relationship between 25(OH)D and CRP levels and cardiovascular diseases based on a representative sample of adult residents of Andijan region and Andijan city of the Republic of Uzbekistan.

4. Conclusions

1. According to our studies, the mean values of SRB were significantly higher than the control group in all groups and regions (*-$P<0.005$; **-$P<0.0001$).
2. A significant inverse correlation between vitamin D, SRB, renin and uric acid content was found in almost all groups of prediabetes patients of both regions ($P<0.005$).

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