CARDIOVASCULAR DISEASE AMONG PATIENTS WITH TYPE 2 DIABETES: ROLE OF HOMOCYSTEINE AS AN INFLAMMATORY MARKER

*ASHOK SAHU[1,2], TRAPTI GUPTA[2], ARVIND KAVISHWAR[3], R. K. SINGH[4]

[1]MGM Medical College Indore, Jabalpur, India;
*e-mail: asahu888@gmail.com; asahu888@yahoo.co.in;
[2]NSCB Medical College, Jabalpur, India;
[3]Regional Malaria Research Centre of Tribal (ICMR), Jabalpur, India;
[4]Chirayu Hospital, Bhopal, India

It is known that inflammation has a role in the pathogenesis of cardiovascular diseases; measurement of inflammatory markers improves the risk prediction of cardiovascular diseases. Hyperhomocysteinemia has been correlated with the occurrence of blood clots, heart attacks and strokes; though it is unclear whether hyperhomocysteinemia is an independent risk factor for these conditions. In the present study, we aimed to evaluate the role of homocysteine in type 2 diabetes patients with cardiovascular disease in a population of Madhya Pradesh India. Total 100 type 2 diabetes patients were included in the study, of these 50 had angiographically proven cardiovascular disease and 50 had no evidence of it. High sensitivity C-reactive protein, fibrinogen, and lipoprotein (a) were measured in serum. Homocysteine, blood glucose in plasma, erythrocyte sedimentation rate, glycated haemoglobin were measured in whole blood. A albumin excretion rate, creatinine clearance rate were measured in the urine sample for renal function. It was shown that, levels of homocysteine and other inflammatory markers were elevated significantly in the group II (n = 50). A correlation between hyperhomocysteinemia and inflammatory markers in patients with impaired renal function was observed. It was concluded that impairment of renal function is a key factor that affects homocysteine level.

K e y   w o r d s: homocysteine, high sensitivity C-reactive protein, lipoprotein (a), creatinine clearance rate, cardiovascular disease, type 2 diabetes, glycated haemoglobin.

Several novel risk factors like interleukin-6, tumor necrosis factor, N type brain natriuretic peptide (NTproBNP) have been proposed as potential criteria for improved detection of subclinical cardiovascular disease [1-3]. In particular, clinical interest has focused on emerging lipid parameters such as lipoprotein(a), on inflammatory markers such as high sensitivity C-reactive protein, fibrinogen, erythrocyte sedimentation rate and homocysteine [1, 4, 5]. Direct comparisons of the magnitude of predictive value associated with each of these parameters have been rare.

Cardiovascular disease (CVD) is considered to be an inflammatory process triggered in response to injury. The increase in inflammatory markers was shown to be related to the risk of cardiovascular disease in diabetic subjects [6, 7].

Several studies demonstrated that plasma homocysteine levels were elevated in diabetes patients [8-10] but the role of inflammatory activity is not well established, the most probable mechanism by which homocysteine induces vascular problem is an alteration of endothelial functions by induction of oxidative stress [11], impaired generation of nitric oxide (NO) [12], decreased vasodilatation, increased proliferation of smooth muscles [13], decreased anticoagulant with suppression of thrombomodulation in endothelial cells [14] and lipid peroxidation [15].

In studies hyperhomocysteinemia is reported as a risk factor for increased risk of CVD in Indians [16, 17]. However, the results of hyperhomocysteinemia in CVD were been conflicting as several other studies had failed to demonstrate an association between homocysteine and CVD in Indians [18, 19]. Therefore, this study was done to evaluate the relationship between the homocysteine levels and CVD in our population.

The present study was undertaken to compare plasma inflammation markers and homocysteine levels in diabetic patients with cardiovascular disease and to investigate possible relationship between inflammatory activity and homocysteine levels in them.

Materials and Methods

The study was a case-controlled in design; we have selected patients as they were presented. The patients included in the present study were all admitted to the intensive coronary care unit (ICCU) or attending the outpatient department of medicine, MGM Medical College and Hospital Indore. Informed consent was obtained from all individual participants included in the study. The Institutional ethical committees of Devi Ahilya Vishwavidyalaya vide their order no. No.Acdm/XI/PhD/Medical Biochemistry/07/496 of DAVV year April 2007 has accorded their approval for the PhD thesis work on the topic entitled "The emerging Role of Novel Markers in Coronary Atherosclerotic Patients with Type-II DM" and the present article is an outcome of the said PhD work.

Consecutive 100 patients undergoing coronary angiography suffering from type 2 diabetes, at our hospital over a period of two years were included in the study. The diagnosis of CVD was made on the basis of clinical history and 12 – lead standard electrocardiogram (ECG) before subjecting them to coronary angiography. The presence of any diameter stenosis ≥ 30% according to coronary angiography using a standard Judkin technique by visual assessment of coronary artery were included in the study as patients ($n = 50$, group II) 45 of them were male and 5 were female, the mean age was observed at (61.32 ± 10.19) and others were excluded and there are no dropouts.

Age and sex matched 50 diabetic subjects as a control (Group I) from medicine outpatient department (OPD) and blood bank with no history of CVD or had normal ECG, were selected for the study. Control had 40 male and 10 female subjects with mean age 52.02 ± 9.47. The name, age, sex, occupation and clinical history were taken on pro forma. Previous histories of diabetes, smoking, hypertension were noted. Fully informed consent was obtained from patients and controls of both groups ($n = 100$).

Exclusion criteria included the use of aspirin, S-adenosylmethionine, vitamin supplements, alcohol, anticonvulsant, estrogens, lipid lowering therapy, other infectious diseases and medications that might affect high sensitivity C-reactive protein (hs-CRP), lipoprotein (Lp(a)) and homocysteine metabolism.

Blood specimens were drawn at 8:00 am after an overnight fast. Samples were centrifuged within 2 h of collection, plasma and serum were separated and frozen immediately at -20 °C [20].

In our study smoking was defined as a regular smoking of cigarettes/beedies [21]. Body mass index (BMI) calculated (kg/m²), patients whose body mass index is ≥25 kg/m², were considered as obese [22]. Blood pressure measured by the person in the sitting position after 5 min rest. A participant was defined as having hypertension if systolic blood pressure was 160 mmHg or more, if the diastolic blood pressure was 95 mmHg or more or if the participant was receiving drug treatment for hypertension [23]. Diabetes mellitus was considered present in patients with a known history of diabetes and in patients with fasting glucose ≥ 126 mg/dl (7.0 mmol/l) according to the World Health Organization (WHO) criteria [24]. A positive family history of CVD was defined as first-degree relative that had documented CVD <55 years in males or <65 years in females. For lipid analysis, samples were obtained after an overnight fast. Patients who had a serum concentration of total cholesterol (TC) ≥ 240 mg/dl, or triglyceride (TG) ≥300 mg/dl, or low-density lipoprotein cholesterol (LDL-C) ≥160 mg/dl or high-density lipoprotein cholesterol (HDL-C) ≤40.0 mg/dl or very-low-density lipoprotein cholesterol (VLDL-C) ≥40.0 are considered as hyperlipedemics [25]. Homocysteine, high sensitivity C-reactive protein, lipoprotein (a) levels ≥ 15.0 mg/dl, ≥1.5 mg/dl, ≥30 mg/dl were considered as higher or increased risk, respectively [26-28].

For the assessment of each parameter we used the commercially available analytical system.

Lipid profile done using serum sample on the fully automatic analyzer by: a) total cholesterol estimated by enzymatic, CHOD/PAP method with cholesterol esterase, cholesterol oxidase and 4-aminoantipyrine, supplied by Roche Diagnostic Ltd.; b) triglyceride estimated by enzymatic, GPO/PAP method with glycerol phosphate oxidase and 4-aminoantipyrine, supplied by Roche Diagnostic Ltd.; c) high density lipoprotein estimated by enzymatic, CHOD/PAP method cholesterol esterase, cholesterol oxidase and N,N-bis (4-sulfobutyl)-m-toludine supplied by Roche Diagnostic Ltd.; d) low density lipo-

protein estimated by enzymatic, CHOD/PAP method with cholesterol esterase, cholesterol oxidase and 4-aminoantipyrine, supplied by Roche Diagnostic Ltd.; e) very low density lipoprotein estimated by enzymatic, CHOD/PAP method, supplied by Roche Diagnostic Ltd.

Fasting blood sugar estimation was done on the fully automatic analyzer using the enzymatic assay kit, plasma as a sample.

Homocysteine assay in the plasma sample done by ELISA, using an enzymatic homocysteine assay manufactured by Bio-Quant, based on novel assay principle that assess the concentration of homocysteine in the sample which is indirectly proportional to the amount of NADH converted to NAD^+ (co-substrate conversion product).

hs-CRP has been done by high sensitivity enzyme immunoassay for quantitative determination of CRP in serum sample, manufacture by BioCheck, Inc. based on solid phase enzyme-linked immunosorbant assay that utilizes a unique monoclonal antibody directed against a distinct antigenic determinant on the CRP molecule.

Lipoprotien(a) in serum sample done by a latex enhanced immunoturbidimetric method using Lp(a) Diazyme's assay kit. Lp(a) present in the sample binds to the specific anti-Lp(a) antibody and causes agglutination, that can be measured optically at 700 nm and is proportional to amount of Lp(a) in the sample.

Blood parameters, fibrinogen, erythrocyte sedimentation rate (ESR) were measured having role in vascular biology and inflammation, fibrinogen estimated by highly sensitive two-site ELISA based on anti FIB antibody, horseradish peroxidase and TMB (tetra methyl benzidine) as chromogenic substrate with a risk of >300 mg/dl value [29], supplied by Alpco Diagnostics. Blood parameter erythrocyte sedimentation rate (ESR) was estimated by blood cell counter having a normal range for male – 14 mm/h, female – 21 mm/h [30].

Urine sample was analyzed for renal function parameter albumin excretion rate (AER) and creatinine clearance rate (Ccr), AER by using Esbach's albuminometer and Ccr by Jaffe reaction.

To ascertain the potential clinical usefulness of each putative risk marker we followed a prior analysis plan. Student '*t*' test was applied to find out the significant difference between two groups. Pearson's correlation analysis was performed between homocysteine and inflammatory marker and between inflammatory markers and other risk factors for their positive or negative association in statistical evaluation. Multiple regression analysis was done for main determinants of homocysteine taken cardiovascular disease as the dependent variable. A *P* value < 0.05 were accepted as indicating a significant statistical analysis were performed using SPSS version 14.3 and the results represented as mean ±SD.

Results and Discussion

Patients were divided in two groups, diabetic associated CVD as group II and without CVD as group I, on the basis of blood glucose or previous history of diabetes and angiographic findings. Baseline data are shown in Table 1. Diabetic subjects with CVD had higher triglyceride, very low density lipoprotein, low HDL-C and albumin excretion rate and from the inflammatory markers diabetic subjects with CVD had higher homocysteine, fibrinogen, hs-CRP, erythrocyte sedimentation rate with *P* < 0.05.

Homocysteine showed a strong positive and significant correlation with AER, triglyceride, haemoglobinA1c (HbA1c), while it was observed negatively correlated with Ccr, HDL-C (*P* < 0.05). The correlation coefficients between the variables were differing significantly among subjects with CVD and in those without CVD when analyzed separately.

In Table 2 we report correlation of inflammatory markers homocysteine, fibrinogen, hs-CRP, erythrocyte sedimentation rate, lipoprotein (a) with other routine CVD risk factors and it was found that homocysteine, fibrinogen, hs-CRP, Lp(a) are inversely related to Ccr and HDL-C, while ESR is negatively correlated with HDL-C and positively with creatinine clearance rate. We have found a significant positive correlation of homocysteine and albumin excretion rate ($r = 0.900$, *P* < 0.01), triglyceride ($r = 0.720$, *P* < 0.01), HbA1c ($r = 0.765$, *P* < 0.01) and significant negative correlation of homocysteine with Ccr ($r = -0.870$, *P* < 0.01), HDL-C ($r = -0.626$, *P* < 0.01) in diabetic subjects with CVD.

We have found a significant positive correlation of homocysteine with other inflammatory marker as shown in Table 3. The results of univariate analysis suggest a role of homocysteine in CVD for further confirmation; we applied multivariate analysis as shown in Table 4, we have found homocysteine as a strong predictor of CVD, T value -4.130, *P* < 0.001. CVD is more prevalent and progresses more rapidly in diabetics in comparison to normal subjects. In the present study, markers of inflammation were found to be significantly elevated in diabetic patients

T a b l e   1. Clinical characteristics and laboratory data of the patients with and without atherosclerotic vascular disease

Risk Factor	Subjects without vascular disease (group I)	Subjects with vascular disease (group II)
Age	52.02 ± 9.47	61.32 ± 10.19
Sex (M/F)	4:1	4.5:0.5
Body Mass Index (BMI)	21.86 ± 2.38	25.43 ± 3.45
Cholesterol, mg/dl	165.26 ± 22.84	287.58 ± 27.35
Triglyceride, mg/dl	183.10 ± 65.20	278.86 ± 46.87
HDL-C, mg/dl	43.28 ± 7.34	28.44 ± 9.02
LDL-C, mg/dl	110.08 ± 29.94	166.36 ± 23.26
VLDL-C, mg/dl	34.74 ± 9.14	45.54 ± 12.199
HbA1c, %	7.00 ± 0.58	9.17 ± 0.97
ESR, ml/h	17.98 ± 1.23	34.39 ± 4.14
Ccr, ml/minx1.73 m^2	79.01 ± 4.50	60.54 ± 6.42
AER, mg/day	49.73 ± 17.08	561.52 ± 128.93
Lp(a), mg/dl	23.52 ± 5.06	63 ± 40.02
hs-CRP, mg/dl	0.530 ± 0.194	1.32 ± 1.45
Fibrinogen, mg/dl	385.51 ± 9.45	461.63 ± 14.171
Homocysteine, μmol/l	6.69 ± 1.60	16.48 ± 1.15

The mean difference is significant statistically at the 0.05 level. HDL-C – high density cholesterol, LDL-C – low density cholesterol, VLDL-C – very low density cholesterol, HbA1c – haemoglobinA1c, ESR – erythrocyte sedimentation rate, Ccr – creatinine clearance, AER – albumin excretion rate, Lp(a) – lipoprotein(a), hs-CRP – high sensitivity C reactive protein, M-male & F-female; $n = 50$, $P < 0.05$.

T a b l e   2. Pearson's correlation coefficient between inflammatory markers, homocysteine level, and other cardiovascular risk factors

Risk Factor → Inflammatory marker↓	Ccr (ml/mx1.73/m^2)	AER (mg/day)	Triglyceride (mg/dl)	HDL-C (mg/dl)	HbA1c (%)
Hcy, μmol/l	$r = -0.870$ $P < 0.01$	$r = 0.900$ $P < 0.01$	$r = 0.720$ $P < 0.01$	$r = -0.626$ $P < 0.01$	$r = 0.765$ $P < 0.01$
Fibrinogen, mg/dl	$r = -0.806$ $P < 0.01$	$r = 0.909$ $P < 0.01$	$r = 0.623$ $P < 0.01$	$r = -0.643$ $P < 0.01$	$r = 0.754$ $P < 0.01$
hs-CRP, mg/dl	$r = -0.253$ $P < 0.05$	$r = 0.376$ $P < 0.01$	$r = 0.256$ $P < 0.01$	$r = -0.155$	$r = 0.264$ $P < 0.01$
Lp(a), mg/dl	$r = -0.492$ $P < 0.01$	$r = 0.496$ $P < 0.01$	$r = 0.382$ $P < 0.01$	$r = -0.394$ $P < 0.01$	$r = 0.370$ $P < 0.01$
ESR, ml/h	$r = 0.792$ $P < 0.01$	$r = 0.867$ $P < 0.01$	$r = 0.596$ $P < 0.01$	$r = -0.655$ $P < 0.01$	$r = 0.732$ $P < 0.01$

The mean difference is significant statistically at the 0.05 level and highly significant at 0.01 levels. Hcy – homocysteine, AER – albumin excretion rate, Lp(a) – lipoprotein (a), hs-CRP – high sensitivity C reactive protein.

T a b l e 3. Pearson correlation coefficients between plasma homocysteine level and inflammation markers

Inflammatory marker→	Fibrinogen	hs-CRP	Lp(a)	ESR
Homocysteine	$r = 0.915$ $P < 0.01$	$r = 0.360$ $P < 0.01$	$r = 0.533$ $P < 0.01$	$r = 0.899$ $P < 0.01$

The mean difference is significant at the $P < 0.05$ level and at $P < 0.01$ is highly significant hs-CRP – high sensitivity C reactive protein, Lp(a) – lipoprotein (a), ESR – erythrocyte sedimentation rate.

T a b l e 4. Main determinants of homocysteine level based on multiple regressions analysis with cardiovascular disease as the dependant variable

Risk Factor	Unstandardized coefficients		Standardized coefficients Beta	T	Sig.	95% CI for B	
	B	Std Error				Lower bound	Upper bound
Age	-0.001	0.001	-0.020	-1.242	0.218	-0.002	0.001
BMI	-0.001	0.003	-0.010	-0.549	0.585	-0.006	0.004
T Cholesterol	-0.001	0.000	-0.089	-2.255	0.027	-0.001	0.000
HDL-C	-0.001	0.001	-0.019	-0.902	0.370	-0.003	0.001
LDL-C	0.000	0.000	-0.015	-0.646	0.520	-0.001	0.000
VLDL-C	-0.001	0.001	-0.013	-0.747	0.457	-0.002	0.001
TG	0.000	0.000	0.031	1.328	0.188	0.000	0.001
HbA1c	-0.056	0.013	-0.153	-4.200	0.000	-0.083	-0.030
Lp(a)	0.000	0.000	-0.002	-1.372	0.174	-0.001	0.000
Hs-CRP	-0.001	-0.001	-0.003	-0.184	0.855	-0.015	0.013
Ccr	0.002	0.001	0.042	1.432	0.156	-0.001	0.005
AER	0.000	0.000	-0.137	-3.498	0.001	0.000	0.000
Fibrinogen	-0.003	0.001	-0.235	-5.762	0.000	-0.004	-0.002
ESR	-0.009	-0.009	-0.150	-3.764	0.000	-0.013	-0.004
(Hcy)	-0.023	0.005	-0.230	-4.130	0.000	-0.033	-0.012

HDL-C – high density cholesterol, LDL-C – low density cholesterol, VLDL-C – very low density cholesterol, HbA1c – haemoglobin A1c, ESR – erythrocyte sedimentation rate, Ccr – creatinine clearance, AER – albumin excretion rate, Lp(a) – lipoprotein(a), hs-CRP – high sensitivity C reactive protein.

with CVD in compression to subjects without CVD. These findings indicate inflammatory activity in study subjects.

Homocysteine level was found to be elevated in patients with vascular disease and was proposed to contribute to atherosclerosis in patients with CVD, stroke and peripheral vascular disease, the pathogenesis behind is: homocysteine induced vascular pathologies including fragmentation of internal elastic lamina, disruption of elastic fibers, smooth muscle hyperplasia and arterial and venous thrombosis [31]. These findings suggest inflammatory activity and role of homocysteine as a risk factor in CVD [32].

Earlier studies on homocysteine reported differences in the level of homocysteine, ranging 13.9-20.1 µmol/l in person with CVD [33, 34] but we have found a mean homocysteine level 16.48 in CVD group II and 6.69 in group I. The homocysteine levels tend to be increased in the presence of other CVD risk factors like age, diabetes, obesity and abnormal lipid parameters and smoking.

Like homocysteine elevated fibrinogen, lipoprotein (a), ESR levels were also found in the present

study, they also have a significant negative correlation with HDL-cholesterol level. It is possible that these inflammatory markers may impair the production or accelerate the catabolism of these lipoproteins that are protective against the atherosclerosis process [35]. It is also seen in the study of Stemme S. et al. in diabetics [36].

Inflammatory markers were shown to be closely related with microalbuminuria and other renal functions that are indicators of renal endothelial injury. However, it is not clear whether inflammation is the cause of nephropathy or inflammatory activity or it is elevated in response to nephropathy [37, 38].

Plasma homocysteine levels are affected directly by the renal functions due to its clearance by the kidney [39]. In the present study homocysteine is having negative significant correlation with Ccr and positive significant correlation with AER. Like homocysteine, fibrinogen, hs-CRP and Lp(a) were also in a significant negative correlation with Ccr.

Of the other inflammatory markers, hs-CRP is the acute phase protein, produced by the liver and marker of systemic inflammation, its elevation in blood may persist in chronic inflammatory conditions. Its production is mediated by interleukin-6 (IL-6), Starling et al. in 2003 reported a positive inverse relationship between hs-CRP and Ccr [40]. This is further supported by studies of PW by de Winter R. J. et al. in atherosclerotic hypertensive patients [41]. Elevated fibrinogen with decreased Ccr suggests that defective coagulation system in the study subjects; this is supported by study of Cateha C et al. [42, 43]. Increased Lp(a) with decreased Ccr are associated with early impairment of renal function and are associated with greater prevalence of CVD, as supported by study in [44, 45].

In literature, both inflammation marker and homocysteine levels were investigated in diabetic patients, but there is no much data of studying their relationship with each other. In our study there is significant relationship found between inflammatory marker and homocysteine levels ($P < 0.01$).

Several recent overview analyses for both homocysteine [45] and lipoprotein (a) [46] had reported statistically significant relationship, according to the study of Eastern et al. [47] there is a significant association of elevated homocysteine and hs-CRP in stenoic coronary arteries. Another study conducted by Aso Y. et al. [48] reported a significant correlation of inflammatory marker hs-CRP, IL-6 and fibrinogen levels with elevated homocysteine levels.

There are some other studies which reported the relationship of homocysteine levels to inflammation in patients with CVD in elderly patients, suggesting a causal relationship between them [49, 50] but they have not taken GFR into the account, this is an important part of study and reflecting that the impairment of renal function is common in patients with prolonged diabetes and old age patients.

As the results of our study show, homocysteine levels have significant association with inflammatory markers and abnormal renal functions in a study of population of diabetics with CVD.

In conclusion, we may state that elevated homocysteine and abnormal renal function are involved in CVD and related complications, i.e. one associated with other and it is difficult to suggest which one initiate and propagate the other. Further study is needed in this direction, taking young patients with diabetes and CVD to understand the exact biochemical mechanism involving, and the role of Hyperhomocysteinemia.

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СЕРЦЕВО-СУДИННІ ЗАХВОРЮВАННЯ У ХВОРИХ НА ЦУКРОВИЙ ДІАБЕТ 2-го ТИПУ: ГОМОЦИСТЕЇН ЯК МАРКЕР ЗАПАЛЕННЯ

Ashok Sahu[1], Trapti Gupta[2], Arvind Kavishwar[3], R. K. Singh[4]

[1]MGM Medical College Indore, Jabalpur, India;
e-mail: asahu888@gmail.com; asahu888@yahoo.co.in;
[2]NSCB Medical College, Jabalpur, India;
[3]Regional Malaria Research Centre of Tribal (ICMR), Jabalpur, India;
[4]Chirayu Hospital, Bhopal, India

Вважається, що запалення відіграють певну роль у патогенезі серцево-судинних захворювань; вимірювання маркерів запалення дозволяє покращити оцінку ризику серцево-судинних захворювань (ССЗ). Гіпергомоцистеїнемія корелює з виникненням тромбів, інфарктів й інсультів, хоча неясно, чи є гіпергомоцистеїнемія

незалежним чинником ризику для цих умов. У роботі досліджували роль гомоцистеїну у хворих на діабет із ССЗ в Індії, штат Мадх'я-Прадеш. Досліджували дві групи хворих на діабет (типу 2): група I ($n = 50$) – без ССЗ і група II ($n = 50$) наявність ССЗ доведена методом ангіографії. У сироватці крові вимірювали С-реактивний протеїн (YS-CRP), фібриноген і ліпопротеїн (a). Також вимірювали вміст гомоцистеїну, глюкози в плазмі, швидкість зсідання еритроцитів та концентрацію глікозильованого гемоглобіну. Рівень екскреції альбуміну і клиренс креатиніну вимірювали в сечі для оцінки роботи нирок. Показано, що рівні гомоцистеїну та інших маркерів запалення були значно підвищені в групі II ($n = 50$) в порівнянні з групою I. Спостерігали кореляцію між гіпергомоцистеїнемією та маркерами запалення в пацієнтів із порушеною функцією нирок. Дійшли висновку про те, що порушення функції нирок є ключовим фактором, який впливає на рівень гомоцистеїну.

К л ю ч о в і   с л о в а: гомоцистеїн (HCY), С-реактивний протеїн (HS-CRP), ліпопротеїни (a), клиренс креатиніну, серцево-судинні захворювання, діабет 2-го типу, глікозильований гемоглобін.

СЕРДЕЧНО-СОСУДИСТЫЕ ЗАБОЛЕВАНИЯ У БОЛЬНЫХ САХАРНЫМ ДИАБЕТОМ 2-го ТИПА: ГОМОЦИСТЕИН КАК МАРКЕР ВОСПАЛЕНИЯ

Ashok Sahu[1], Trapti Gupta[2], Arvind Kavishwar[3], R. K. Singh[4]

[1]MGM Medical College Indore, Jabalpur, India;
e-mail: asahu888@gmail.com; asahu888@yahoo.co.in;
[2]NSCB Medical College, Jabalpur, India;
[3]Regional Malaria Research Centre of Tribal (ICMR), Jabalpur, India;
[4]Chirayu Hospital, Bhopal, India

Считается, что воспаление играет определенную роль в патогенезе сердечно-сосудистых заболеваний; измерение маркеров воспаления позволяет улучшить оценку риска сердечно-сосудистых заболеваний (ССЗ). Гипергомоцистеинемия коррелирует с возникновением тромбов, инфарктов и инсультов, хотя неясно, является ли гипергомоцистеинемия не-

зависимым фактором риска для этих условий. В работе исследовали роль гомоцистеина у больных диабетом с ССЗ в Индии, штат Мадхья-Прадеш. Исследовали две группы больных диабетом (тип 2): группа I ($n = 50$) – без ССЗ и группа II ($n = 50$) – наличие ССЗ доказано методом ангиографии. В сыворотке крови измеряли С-реактивный протеин (YS-CRP), фибриноген и липопротеин (a), а также уровень гомоцистеина, глюкозы в плазме, скорость оседания эритроцитов, концентрацию гликозилированного гемоглобина. Уровень экскреции альбумина и клиренс креатинина измеряли в моче для контроля работы почек. Показано, что уровни гомоцистеина и других маркеров воспаления были значительно повышены в группе II ($n = 50$) по сравнению с группой I. Наблюдали корреляцию гипергомоцистеинемии и воспалительных маркеров в группе пациентов с нарушенной функцией почек. Сделан вывод о том, что нарушение функции почек является ключевым фактором, который влияет на уровень гомоцистеина.

К л ю ч е в ы е   с л о в а: гомоцистеин (HCY), С-реактивный протеин (HS-CRP), липопротеины (a), клиренс креатинина, сердечно-сосудистые заболевания, диабет 2-го типа, гликозилированный гемоглобин.

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