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ORIGINAL RESEARCH

A Study on Association of Serum Homocysteine and Lipid Profile in Patients with Type 2 Diabetes Mellitus

Vijaitha SM[1], Sapna Vyakarnam[2], Aparna Varma Bhongir[3]

[1]Assistant Professor, Department of Biochemistry, Govt Medical College, Jagityal, Telangana, India.

[2]Professor &HOD, Department of Biochemistry, Mediciti Institute of Medical Sciences, Ghanpur, Telangana, India.

[3]Additional Professor, Department of Biochemistry, AIIMS, Bibinagar, Telangana, India.

ABSTRACT

Background: Diabetes mellitus (DM) is a condition that affects many people and has reportedly spread worldwide. Numerous problems, including as cardiovascular disease (CVD), nephropathy, neuropathy, and retinopathy, develop over time as a result of long term diabetes. Poor glycemic management and endothelial dysfunction are the causes of these complications. Any metabolite that has an atherosclerotic character may aid in the emergence of such long-term problems. It has been established that dyslipidemia and hyperhomocysteinemia are separate indicators of atherosclerosis. However, there is much disagreement over how they interact and affect insulin metabolism. Analyzing the relationship between these risk factors may be useful in reducing complications and lengthening the lifespan of diabetes patients. Aim: The purpose of the current study was to investigate the relationship between homocysteine and the lipid profile and glycated haemoglobin components in type II diabetes patients. Diabetes patients' serum homocysteine and lipid profile levels were also contrasted with those of non-diabetic, healthy participants.

Results: Lipid profile and serum homocysteine were shown to be strongly correlated. Low density lipoprotein (LDL) and S. cholesterol levels were shown to be greater in diabetic individuals with hyperhomocysteinemia. In individuals with HbA1c levels > 8.0 percent, S. homocysteine was also discovered to be high, which is a sign of poor glycemic management. S. homocysteine, cholesterol, triglycerides, LDL, and very low-density lipoprotein (VLDL) were all considerably higher in diabetes patients as compared to healthy people.

Conclusion: Patients with type II diabetes are highly advised to undergo routine testing for hyperhomocysteinemia and the serum lipid profile. Proper patient treatment can help to prevent the emergence of numerous problems and improve quality of life by reducing cholesterol levels, hyperhomocysteinemia, and maintaining a strong glycemic control.

Keywords: Diabetes mellitus, Glycemic control, Homocysteine, Hyperhomocysteinemia, and Lipid profile.

Corresponding Author: Dr. Vijaitha SM, Assistant Professor, Department of Biochemistry, Govt Medical College, Jagityal, Telangana, India

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INTRODUCTION

A category of metabolic illnesses known as diabetes mellitus are characterised by persistently increased blood sugar levels. Its prevalence was predicted to be 8% globally in 2011 and is projected to increase to 10% by the year 2030.[1,2]

The "Diabetic Capital of the World" is regarded as being in India. By 2030, it is predicted that 366 million people worldwide would have diabetes, according to Wild et al.[3] Additionally, up to 79.4 million of the aforementioned diabetes people are predicted to be from India. Diabetes mellitus is primarily characterised by chronic hyperglycemia and is brought on by abnormalities in insulin secretion, action, or both.[4]

Type II diabetes, also known as noninsulin-dependent DM, is brought on by an insufficient supply of insulin and a decrease in the potency of the insulin that is generated. This illness develops more gradually and is more prevalent in those over 40. Type II diabetes affects around 90% of diabetics. Diabetes and insulin resistance are thought to have a substantial correlation with the emergence of numerous cardiovascular morbidities and problems. The risk of coronary artery disease, post-myocardial infarction morbidity, and acute myocardial infarction mortality are all thought to be two to three times greater in diabetic patients than in non-diabetic individuals. Type II diabetes and premature atherosclerosis frequently go hand in hand.[5,6]

Numerous studies have shown a favourable correlation between poorly controlled diabetes, hyperinsulinemia, polycystic ovaries, obesity, hypertension, smoking, sedentary lifestyle, and specific ethnic groups and glucose intolerance. These characteristics, however, are insufficient to support the substantial link between diabetes and early atherosclerosis. Homocysteine, an intermediate amino acid that contains sulphur, is now known to be a substantial contributor to atherosclerosis and arteriosclerosis. It is created as a byproduct of the process that turns methionine into cysteine. Through a number of mechanisms, including vascular endothelium damage, stimulation of smooth muscle cell proliferation, increased low density lipoprotein cholesterol (LDL-C) peroxidation, and thrombosis activation, hyperhomocysteinemia (HHcy) has been recognised as a new modifiable risk factor for cardiovascular disease (CVD).[7]

Few studies have demonstrated that having type II diabetes with poor glycemic control increases the risk of atherosclerosis and cardiovascular disease (CVD). As an independent and significant predictor of complications in DM, particularly atherothrombotic events, homocysteine has been suggested.[8,9] HHcy may also make people with dyslipidemia more susceptible to CVD. Recent studies have clearly shown the significance of the metabolic balance between S-adenosylmethionine (SAM), S-adenosylhomocysteine (SAH), phosphatidylcholine (PC), phosphatidylethanolamine (PE), and choline in Hcy metabolism, hypolipoproteinemia, liver function, and CVD, even though the mechanism of the link is not fully understood. Numerous investigations linking HHcy to abnormal HDL-C metabolism shown that Hcy can lower blood levels of HDL by preventing the formation of ApoA-I protein and increasing HDL-C clearance.[10,11]

It is more common for diabetic individuals with macroangiopathy and nephropathy to have high homocysteine levels. The connection between macroangiopathy, renal disease, and hyperhomocysteinemia in type II diabetes has not yet been determined. Serum homocysteine levels and type II diabetes is currently the subject of intense discussion. Plasma homocysteine levels and insulin levels or insulin resistance have been found to positively correlate in several investigations. Furthermore, it has been shown that insulin prevents the trans-sulfuration pathway's conversion of homocysteine to cysteine. According to several studies, increasing lipid peroxidation is linked to elevated homocysteine levels in blood.[12,13,14] Lipid-lowering medications may be useful for treating endothelial dysfunction in people with

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hyperhomocysteinemia, according to some research. In order to determine the likelihood of developing CVD and atherosclerosis in type II diabetic individuals, it may be useful to examine the relationship between blood homocysteine levels and other lipid profile components. Therefore, the goal of the current study is to examine how blood lipids and homocysteine are related in type II diabetes patients.[15,16]

MATERIALS & METHODS

The current study included 100 newly diagnosed type II DM patients, aged up to 65, who were seen by the outpatient department of medicine. As a control group, 50 healthy participants of either sex or similar age were enlisted in the research. Patients older than 65, those with serious liver or kidney illness, and those on lipid-lowering medications were not allowed to participate in the trial. All participants in the case and control groups provided written permission. The individuals' full medical histories were obtained, and a comprehensive physical examination was carried out. After an overnight fast, blood samples were drawn via venipuncture under aseptic conditions. Fasting blood sugar levels, serum homocysteine levels, and the serum lipid profile, which includes serum cholesterol and triglycerides, were all examined in the samples high-density lipoprotein (HDL), LDL and VLDL. All chemical assays were performed using ortho-clinical diagnostics reagents on dry chemistry analyzer VITROS 4600. The data obtained for each analyte were presented as mean ± SD. Values of diabetic and control group were compared by applying Student’s t-test. The diabetic group was further categorized based on the homocysteine levels as normal and hyperhomocysteinemia. Components of lipid profile were compared among these subgroups.

RESULTS

50 healthy, normal volunteers and 100 type II DM patients participated in the current investigation. The control group's participants were asymptomatic individuals who had no abnormalities on regular evaluation. The individuals' average ages in the control and diabetes groups were compared. The control group's mean age is 55.2 ± 10.84 years, whereas the diabetes group's is 54.1 ± 16.1 years.

The diabetic group's mean fasting blood glucose level was found to be considerably higher ($p = 0.000$). In comparison to the control group, which had a mean serum homocysteine content of 10.3 ± 3.22 mol/L, the diabetic group's was much higher at 21.21 ± 7.62 mol/L.

The lipid profile's various components were also contrasted between the two groups. In the current study, the mean blood total cholesterol concentration in the control group was 156.24 ± 26.20 mg/dL, but the mean serum total cholesterol in the diabetes patients group was considerably higher ($p = 0.000$), coming in at 176.5 ± 41.8 mg/dL. In the diabetes group compared to the control group, the amount of serum TG was likewise considerably higher ($p = 0.000$). The Fried Wald equation was used to determine the serum levels of LDL and VLDL cholesterol. In the patients with diabetes, mean values for both LDL and VLDL exhibited a substantial fluctuation with higher mean values.

Although a significant difference in HDL cholesterol levels was not seen, type II diabetes individuals did have a slightly lower amount.

Additionally, the blood homocysteine levels were used to divide the 100 diabetes participants into smaller groups. Hyperhomocysteinemia is defined as serum homocysteine levels >15.0 mol/L; 30 individuals with type II diabetes mellitus had homocysteine levels 15.0 mol/L and 70 had homocysteine levels >15.0 mol/L. The mean blood sugar levels in the two subgroups were almost identical and showed no discernible change.

When the blood lipid profiles of the two subgroups were compared, it was found that the subgroup with hyperhomocysteinemia had a significantly higher level of serum cholesterol

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and LDL-cholesterol. In connection to glycemic management, serum homocysteine levels in diabetic individuals were also compared.

60 of the 100 diabetic research participants had their HbA1c levels checked; this test is a solid indicator of glycemic management. Serum homocysteine levels in patients with poor glycemic control (HbA1c > 8.0%) were found to be considerably higher.

Table 1: Comparison of variables in both study groups

Variable	DiabetesPatients (N=50)	Controls (N=50)	P Value
Age (years)	55.2 ± 10.84	54.1 ± 16.1	NS
Blood sugar fasting (mg/dL)	248.60 ± 70.2	99.8 ± 14.62	0.000
S. homocysteine (µmol/L)	21.21 ± 7.62	10.3 ± 3.22	0.000
S. cholesterol (mg/dL)	176.5 ± 41.8	156.24 ± 26.20	0.000
S. triglycerides(mg/dL)	142.0 ± 64.2	112.12 ±43.25	0.000
S. HDL-Chol (mg/dL)	41.0 ± 9.44	45.22 ± 6.88	NS
S. LDL-Chol (mg/dL)	101.0 ± 31.7	82.12 ± 20.50	0.000
S. VLDL-Chol (mg/dL)	29.89 ± 13.66	24.26 ± 8.32	0.000

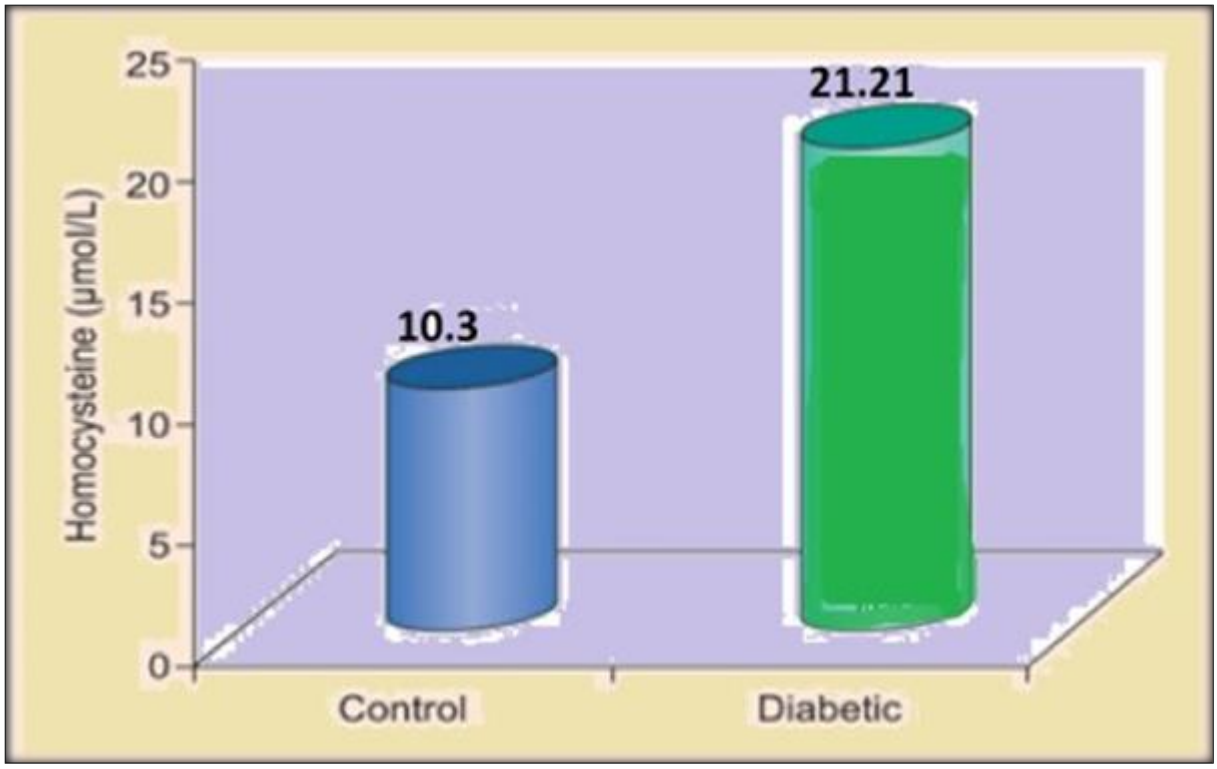

Figure 1: Comparison of homocysteine (µmol/L) between control and patient group

Table 2: Distribution of variables between normal and hyperhomocysteinemia subgroups

Variable	S. homocysteine >15 µmol/L (n = 73)	S. homocystein e ≤15 µmol/L (n = 27)	P Value
Blood sugar fasting (mg/dL)	247.9 ± 69.12	242.8 ± 74.10	NS
S. homocysteine (µmol/L)	22.0 ± 6.5	12.42 ± 1.22	0.000
S. cholesterol (mg/dL)	185.0 ± 42.2	150.22 ± 35.55	0.003
S. triglycerides(mg/dL)	151.0 ± 72.0	136.8 ± 58.2	NS
S. HDL-Chol (mg/dL)	41.5\48 ± 9.42	40.25 ± 8.56	NS

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S. LDL-Chol (mg/dL)	108.6 ± 30.42	82.45 ± 28.82	0.000
S. VLDL-Chol (mg/dL)	30.10 ± 14.38	26.25 ± 11.52	NS

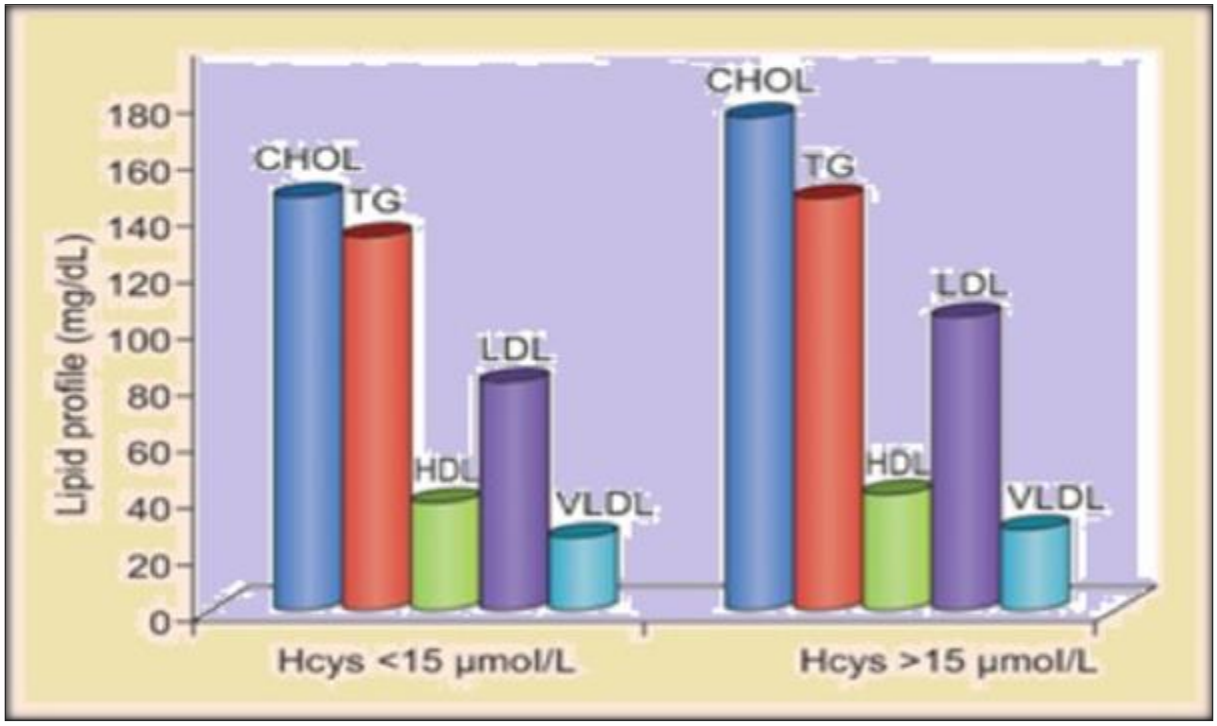

Figure 2: Comparison of lipid profile (mg/dL) based onhomocysteine group

Table 3: Distribution of S. homocysteine based on the HbA1c in type II diabetic patients

Variables	HbA1c ≤8.0% (n = 22)	HbA1c> 8.0% (n = 37)	p value
S. homocys tei ne	18.88 ± 6.27	22.14 ± 8.24	0.035
(µmol/L)			

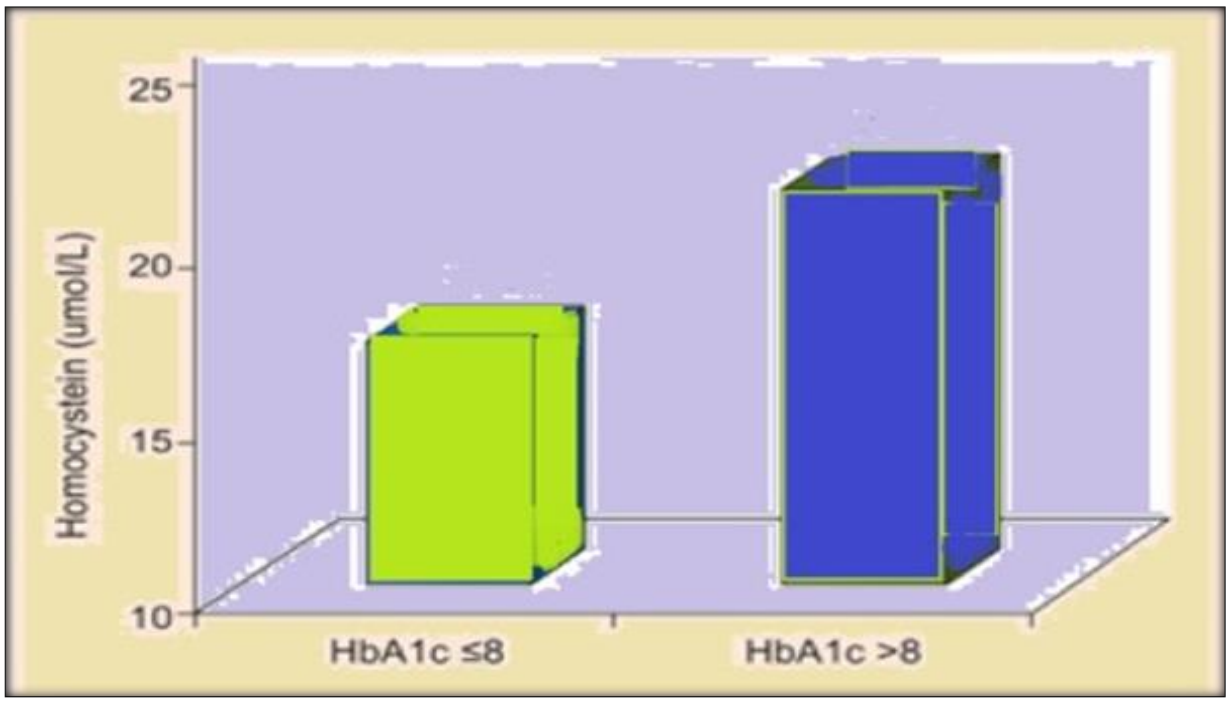

Figure 3: Comparison of S. homocysteine (µmol/L) based onHbA1c group

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DISCUSSION

Diabetes mellitus is a worldwide health issue since it is one of the primary causes of morbidity and death. Furthermore, this disease's consequences have a negative impact on people's quality of life.[14] Demethylation of methionine as a cofactor during its conversion to cysteine results in the formation of homocysteine, a sulfur-containing non-essential amino acid. It is now acknowledged as a significant arteriosclerosis risk factor. A prominent risk factor for atherosclerotic disease in both diabetic and non-diabetic patients is hyperhomocysteinemia, which is defined as increased homocysteine levels in plasma, typically >15.0 mol/L. Chronic vascular problems in diabetic people with hyperhomocysteinemia may arise. Although there have been several studies on the significance of homocysteine in diabetes patients, it is still unclear how hyperhomocysteinemia and cardiovascular risk are related. The state of the DM affects many systems involved in lipid metabolism. Diabetes-induced dyslipidemia, notably a rise in the LDL component, may be to blame for the higher prevalence of coronary heart disease (CHD) among diabetics. The purpose of the current study was to assess the relationship between homocysteine and other lipid profile elements in diabetes individuals. Serum homocysteine levels in diabetic individuals were over 15 mol/L in 73% of cases. Elevated homocysteine levels have been linked to a wide variety of medical conditions, including CVD, stroke, etc. The diabetic group in the current study had significantly higher levels of the lipid profile components cholesterol, TG, LDL, and VLDL than did the control group. In a related investigation, Sniderman et al. found that hypertriglyceridemia was associated with high levels of tiny, dense LDL particles and low levels of HDL cholesterol.[16] Numerous studies have shown a positive correlation between glucose intolerance and CVD in the presence of obesity, dyslipidemia, hypertension, polycystic ovarian syndrome, smoking, sedentary lifestyle, certain ethnic groups, poorly controlled diabetes, and hyperinsulinemia due to any cause or risk factors. However, not all of these causes can account for the substantial link between diabetes and early atherosclerosis. Previous investigations have shown that type-II DM patients had hyperhomocysteinemia, which may play a role in the onset of vascular complications.[17,18,19] Wijekoon et al,[20] claim that a rise in plasma homocysteine levels has been recognised as a risk factor for a number of illnesses, including CVD. In addition to the transsulfuration enzymes, the betaine homocysteine methyl transferase enzyme was found to have a significant role in the enhanced catabolism of homocysteine in type II diabetes. Serum homocysteine levels that are elevated have been linked to CHD status. Hyperhomocysteinemia's role in type II diabetes is difficult to explain. It might be challenging to consider reduced renal function in several ways, including decreased creatinine clearance, albuminuria, or both25–29. According to Puri et al.,[21] diabetic patients' mean homocysteine levels were nearly twice as high as those of the controls. Homocysteine levels in patients were >18 mol/L in 72.55 percent of cases, compared to >18 mol/L in controls in only 26.67 percent of cases. These results are consistent with the findings of the current study, which found that 73 percent of the patients in the diabetic group had homocysteine levels over 15.0 mol/L. Homocysteine levels were 28.86 13.02 mol/L in the hyperlipid subgroup of the aforementioned research and 26.46 13.44 mol/L in the normolipid subgroup. Therefore, there was no discernible difference between the homocysteine levels and the lipid profile.

The two metabolic processes that break down homocysteine are trans-sulfuration and re methylation, according to Abraham et al.[22] Homocysteine thiolactone is a significant by-product formed when there is too much homocysteine in the blood circulation. The macrophages entrap this byproduct, which is then integrated into foam cells to form the first atherosclerotic plaques. Homocysteine thiolactone acylates the proteins and alters the

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oxidative functions of the arteries inside these plaques. In turn, this encourages atherothrombosis. Additionally, the oxidation of homocysteine produces superoxide and hydrogen peroxide. As a result of endothelial dysfunction, which further encourages the proliferation of blood vessel smooth muscles, such oxygen-derived molecules may contribute to the oxidation of LDL. In the current investigation, the diabetic subgroup with hyperhomocysteinemia had higher blood cholesterol and LDL values. According to Durdi et al.,[23] there was a substantial positive association between total Hcy and LDL-C and a negative correlation between total Hcy and HDL-C in 126 individuals who had myocardial infarction. Hcy was discovered to be favourably linked with TG and VLDL-C and negatively associated with HDL-C in 300 Indian patients with established coronary heart disease.[24] Low HDL levels were related with the MTHFR TT genotype and Hcy ($r = 0.370$, $P = 0.003$) in 125 individuals with heterozygous familial hypercholesterolemia.[25] Each of these dyslipidemic characteristics, according to Krauss,[26] is linked to a higher risk of CVD. The probable aetiology of this dyslipidemia may involve increased hepatic production of TGs rich in VLDL and its poor clearance. Specific big VLDL precursors undergo intravascular processing to become small, dense LDL particles. Ronald et al.[27] showed that insulin resistance and hyperglycemia are the causes of lipid abnormalities. In 60 patients with ischemic heart disease, Yadav,[28] observed that there was no statistically significant association between plasma Hcy and TC, HDL-C, and TG. 155 diabetic individuals were included in a study that discovered no connection between Hcy and lipids. In the highest Hcy quartile, levels of TG and VLDL-C were greater than levels of LDL-C, non-HDL-C, and HDL-C in uncorrected analysis, but these relationships vanished after controlling for confounders, according to the most recent data, which included 18297 US individuals.[29] Similarly, Tushuizen et al,[30] discussed that high postprandial blood sugars and high lipid levels are risk factors for vascular diseases.In another study by Shera et al,[31] it was proposed that uncontrolled diabetes may lead to higher macro as wellas microvascular complications and is further relatedto longer duration of disease, poor glycemic control, increased body weight, and hypertension. The vascularcomplications were ischemic heart disease, myocardial infarction, and cerebrovascular accident. Thus, the overall results of this study suggest that type II diabetes individuals have much higher homocysteine levels, which may be a factor in the development of endothelial dysfunction and associated problems. Dyslipidemia follows hyperhomocysteinemia and vice versa. The homocysteine levels in these individuals appear to be influenced by glycemic management as well. The study advises more investigation into the relationship between glycemic control and hyperhomocysteinemia in larger patient populations. According to the study, preventing hyperhomocyst einemia and its consequences may be possible with effective counselling and maintenance of a healthy lifestyle that ensures good glucose management and a balanced lipid profile.

CONCLUSION

According to the current study, those with type II diabetes run the risk of acquiring hyperhomocysteinemia and dyslipidemia. While dyslipidemia is predictive of cardiovascular problems, homocysteine is a measure of endothelial dysfunction. Therefore, assessing these risk factors might be useful in identifying individuals who are likely to experience severe issues early on. Long-term diabetes can cause serious consequences, but leading a healthy lifestyle and keeping a strong glycemic control can help with patient care and prevent the development of such difficulties. As part of the screening and follow-up of type II diabetes patients, estimation of serum homocysteine and serum lipid profile is thus advised. Folic acid and vitamin B12 supplements can reduce serum homocysteine levels. Proper patient counselling, particularly on adopting a healthy lifestyle that includes a balanced diet and regular exercise, can be very effective in managing dyslipidemia. The findings call for more

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investigation into the relationship between homocysteine and other inflammatory markers in type II diabetes patients.

REFERENCES

1. Baynest HW. Classification, pathophysiology, diagnosis and management of diabetes mellitus. J Diabetes Metabol 2015;6(5):1-9.
2. International Diabetes Federation (IDF). Country estimates table 2011. IDF Diabetes Atlas, 2012. p. 6.
3. Wild S, Roglic G, Green A, Sicree R, King H. Global prevalence of diabetes—estimates for the year 2000 and projections for 2030. Diabetes Care 2004 May;27(3):1047-1053.
4. American Diabetes Association. Diagnosis and classification of diabetes mellitus Diabetes Care 2005 Jan;1(suppl 1):537-542.
5. Lehto S, Ronnemaa T, Pyorala K, Laakso M. Cardiovascular risk factors clustering with endogenous hyperinsulinaemia predict death from coronary heart disease in patients with type II diabetes. Diabetologia 2000 Feb;43(2):148-155.
6. Haffner SM, Lehto S, Ronnemaa T, Pyorala K, Laakso M. Mortality from coronary heart disease in subjects with type 2 diabetes and in nondiabetic subjects with and without prior myocardial infarction. N Engl J Med 1998 Jul;339(4):229-234.
7. Antoniades C, Antonopoulos AS, Tousoulis D, Marinou K, Stefanadis C. Homocysteine and coronary atherosclerosis: from folate fortification to the recent clinical trials. Eur Heart J. 2009;30(1):6–15. doi: 10.1093/eurheartj/ehn515.
8. Obeid R, Herrmann W. Homocysteine and lipids: S-adenosyl methionine as a key intermediate. FEBS Lett. 2009;583(8):1215–25. doi: 10.1016/j.febslet.2009.03.038. [Abstract] [CrossRef] [Google Scholar]
9. Xiao Y, Zhang Y, Lv X, et al. Relationship between lipid profiles and plasma total homocysteine, cysteine and the risk of coronary artery disease in coronary angiographic subjects. Lipids Health Dis. 2011;10:137. doi: 10.1186/1476-511X-10- 137. [Europe PMC free article] [Abstract] [CrossRef] [Google Scholar]
10. Herrmann W, Obeid R, Hubner U, Jouma M, Geisel J. Homocysteine in relation to C reactive protein and low-density lipoprotein cholesterol in assessment of cardiovascular risk. Cell Mol Biol (Noisy-le-grand) 2004;50(8):895– 901. [Abstract] [Google Scholar]
11. Daly C, Fitzgerald AP, O'Callaghan P, Collins P, Cooney MT, Graham IM. Homocysteine increases the risk associated with hyperlipidaemia. Eur J Cardiovasc Prev Rehabil. 2009;16(2):150–5. doi: 10.1097/HJR.0b013e32831e1185. [Abstract] [CrossRef] [Google Scholar]
12. Gallistl S, Sudi K, Managge H. Insulin is an independent cor relate of plasma homocysteine levels in obese children and adolescents. Diabetes Care 2000 Sep;23(9):1348-1352.
13. Sainani GS, Karatela RA. Plasma leptin in insulin-resistant and insulin-nonresistant coronary artery disease and its associa tion with cardio-metabolic risk factors among Asian Indians. Metab Syndr Relat Disord 2009 Aug;7(4):335-340.
14. Chiang EP, Wang YC, Chen WW, Tang FY. Effects of insulin and glucose on cellular metabolic fluxes in homocysteine transsulfuration, remethylation, S adenosylmethionine syn thesis, and global deoxyribonucleic acid methylation. J Clin Endocrinol Metab 2009 Mar;94(3):1017-1025.
15. Li H, Lewis A, Brodsky S, Rieger R, Iden C, Goligorsky MS. Homocysteine induces 3-hydroxy-3-methylglutaryl coenzyme A reductase in vascular endothelial cells: a mechanism for development of atherosclerosis? Circulation 2002 Mar;105(9): 1037-1043.

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16. Sniderman AD, Scantlebury TH, Cianflone K. Hypertriglyc eridemic hyperapo B: the unappreciated atherogenic dysli poproteinemia in type 2 diabetes mellitus. Ann Intern Med 2001 Sep;135(6):447-459.
17. El Oudi M, Aouni Z, Ouertani H, Mazigh C, Machghoul S. Effect of lipopenic and hypotensive treatment on homocyst eine levels in type 2 diabetics. Vascular Health Risk Manag 2010 May;6:327-332.
18. Ebseunun MO, Obajobi EO. Elevated plasma homocysteine in type 2 diabetes mellitus: a risk factor for cardiovascular diseases. Pan Afr Med J 2012;12:48.
19. Kajbaf F, Ghaffari MA, Kajbaf MJ. Reduced serum homocyst eine levels in diabetic patients. Iran J Pathol 2012;7(1):14-18
20. Wijekoon EP, Brosnan ME, Brosnan JT. Homocysteine metabolism in diabetes. Biochem Soc Trans 2007 Nov;35(Pt 5): 1175-1179.
21. Puri A, Gupta OK, Dwivedi RN, Bharadwaj RPS, Na-rain VS, Singh S. Homocysteine and lipid levels in young patients with coronary artery disease. J Assoc Phys India 2003 Jul;51:681-685.
22. Abraham JM, Cho L. The homocysteine hypothesis: still relevant to the prevention and treatment of cardiovascular disease? Cleve Clin J Med 2010 Dec;77(12):911-918.
23. Qujeq D, Omran TS, Hosini L. Correlation between total homocysteine, low-density lipoprotein cholesterol and high-density lipoprotein cholesterol in the serum of patients with myocardial infarction. Clin Biochem. 2001;34(2):97–101. doi: 10.1016/S0009-9120(01)00187-4. [Abstract] [CrossRef] [Google Scholar]
24. Mahalle N, Kulkarni MV, Garg MK, Naik SS. Vitamin B12 deficiency and hyperhomocysteinemia as correlates of cardiovascular risk factors in Indian subjects with coronary artery disease. J Cardiol. 2013;61(4):289–94. doi: 10.1016/j.jjcc.2012.11.009. [Abstract] [CrossRef] [Google Scholar]
25. Real JT, Martinez-Hervas S, Garcia-Garcia AB, et al. Association of C677T polymorphism in MTHFR gene, high homocysteine and low HDL cholesterol plasma values in heterozygous familial hypercholesterolemia. J Atheroscler Thromb. 2009;16(6):815–20. doi: 10.5551/jat.2196. [Abstract] [CrossRef] [Google Scholar]
26. Krauss RM. Lipids and lipoproteins in patients with type 2 diabetes. Diabetes Care 2004 Jun;27(6):1496-1504.
27. Ronald M. Lipid and lipoproteins in type 2 diabetes. Diabetes Care 2004 Jun;27(6):1496-1504.
28. Yadav AS, Bhagwat VR, Rathod IM. Relationship of plasma homocysteine with lipid profile parameters in ischemic heart disease. Indian J Clin Biochem. (2006) 21:106–10. 10.1007/bf02913076
29. Lupton JR, Quispe R, Kulkarni K, Martin SS, Jones SR. Serum homocysteine is not independently associated with an atherogenic lipid profile: The Very Large Database of Lipids (VLDL-21) study. Atherosclerosis. 2016;249:59–64. doi: 10.1016/j.atherosclerosis.2016.03.031. [Abstract] [CrossRef] [Google Scholar]
30. Tushuizen M, Diamant M, Heine R. Postprandial dysmetabo lism and cardiovascular disease in type 2 diabetes. Postgrad Med J 2005 Jan;81(951):1-6.
31. Shera A, Jawad F. Prevalence of chronic complications and associated factors in Type 2 Diabetes. J Pak Med Assoc 2004 Feb;54(2):54-59.