COMPARISON OF LIPID PROFILE IN PATIENTS WITH DIABETIC NEUROPATHY AND WITHOUT NEUROPATHY; A CROSS SECTIONAL STUDY

Kanwal Huma, Khadija Mehboob, Amir Rashid, Fatima Fuad*, Muhammad Mamoon Mujahid, Asma Arshad*****

Army Medical College/National University of Medical Sciences (NUMS) Rawalpindi Pakistan, *Islamabad Medical and Dental College, Islamabad Pakistan, **Pak Emirates Military Hospital/National University of Medical Sciences (NUMS) Rawalpindi Pakistan, ***Combined Military Hospital Lahore/National University of Medical Sciences (NUMS) Pakistan

ABSTRACT

Objective: To compare lipid profile in patients with diabetic neuropathy and without neuropathy.
Study Design: Cross-sectional comparative study.
Place and Duration of Study: This study was carried out at Multidisciplinary Lab-1, Department of Biochemistry and Molecular Biology, Army Medical College, from Jan 2020 to Sep 2020 in collaboration with Pak-Emirates Military Hospital, Rawalpindi.
Methodology: Eighty-four subjects were selected and divided into three groups, twenty-eight in each. Group I included diagnosed patients with type 2 diabetes mellitus with peripheral neuropathy, group II included diagnosed patients with type 2 diabetes mellitus without peripheral neuropathy and group III consisted of healthy individuals. Biochemical parameters including total cholesterol, triglycerides, high density lipoprotein cholesterol and low density lipoprotein cholesterol were measured. Data was analyzed by SPSS version 22.0. One way ANOVA test was used that followed by post-Hoc Tukey test for group comparison.
Results: There was significant difference in triglycerides (*p*-value 0.001) and high density lipoprotein cholesterol (0.003) levels among group I and III. While, between group II and III significant difference of high density lipoprotein cholesterol was present. There was no significant difference between group I and II regarding all lipid profile parameters.
Conclusion: There was significant increase of triglycerides levels and decrease of high density lipoprotein cholesterol in patients with diabetic peripheral neuropathy as compared to healthy controls. No significant difference was observed for all parameters of lipid profile between patients with diabetic peripheral neuropathy and without peripheral neuropathy.

Keywords: Diabetic peripheral neuropathy, Lipid profile, Type 2 diabetes mellitus.

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INTRODUCTION

Diabetes mellitus (DM) is a complex, chronic metabolic disorder recognized as of the top ten causes of deaths in adults. Around 463 million individuals are currently living with DM worldwide. This number will further increase up to 578 million in 2030. The prevalence of DM in Pakistan is 19.4% and the country is ranked fourth among top ten countries with DM. Moreover, Pakistan is expected to surpass the United States of America, and move to third place by 2045[1]. Long-standing type 2 diabetes mellitus with poor glycemic control eventually causes macrovascular and microvascular complications such as neuropathy, nephropathy and retinopathy[2].

Diabetic neuropathies are most common microvascular complications as they affect approximately 30-90% of DM patients in the world[3]. According to American diabetes association, there are three main types of diabetic neuropathy. These are diffuse neuropathy, mononeuropathy (mononeuritis multiplex) and radiculopathy or polyradiculopathy. Among diffuse neuropathies, distal symmetrical peripheral neuropathy (DSPN) is most common variety and generally referred to as diabetic peripheral neuropathy (DPN) or diabetic neuropathy (DN). So, the present study is focused on diabetic peripheral neuropathy. DPN is present in 10-15% of patients with type II diabetes mellitusat time of their diagnosis and this rate is further increased up to 50%

Correspondence: Dr Kanwal Huma, Biochemistry Department, Army Medical College Rawalpindi Pakistan
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after 10 years of their diagnosis of DM[4]. It is defined as symmetrical, length-dependent sensory-motor polyneuropathy that is caused by microvasculature and metabolic alterations as a result of chronic hyperglycemia[5].

Hyperglycemia, insulin resistance and dyslipidemia are main pathological factors that involved in nerve dysfunction and cellular death in diabetic neuropathy. They activate multiple biochemical pathways such as polyol, hexosamine pathways and loss of insulin signaling, which cause oxidative stress, inflammation and mitochondrial dysfunction and alter gene expression. These altered metabolic changes not only affect nerves but also disturb mitochondrial redox balance and increased production of mitochondrial and cytosolic reactive oxygen species[6]. While, hyperlipidemia causes production of pro-inflammatory substances from adipocytes[7].

Many studies reported the dyslipidemia in patients with type 2 DM is characterized by elevated levels of triacylglycerol and reduced levels of high-density lipoprotein (HDL) cholesterol and these alterations may be reported several years before the clinical detection of hyperglycemia[8]. Increased triacylglycerol levels are associated with development of neuropathy in type 2 diabetes while obesity is independently correlated with development of neuropathy. Some studies report that lipid lowering drugs reduce the risk of lower-limb amputations, which is one of the most serious and life altering complications of diabetic neuropathy[9].

Deranged lipid profile in patients with diabetes mellitus result either of diabetic complication or as a risk factor for diabetes development acts in harmony with oxidative stress and chronic hyperglycemia to produce pathological alterations in different cells of peripheral nervous system including dorsal root ganglion neurons, neuronal axons and schwann cells. Due to contributory role of dyslipidemia in pathogenesis diabetic peripheral neuropathy, there is earlier incidence of peripheral neuropathy in type 2 was observed as compared to type 1 diabetes mellitus[10].

In more than 50% of patients with diabetic neuropathy, irreversible nerve damage has been occurred prior to diagnosis. That leads to increase number of diabetes related hospital admission and limb amputations. Currently there is no effective treatment is present that completely cure diabetic neuropathy. So, research on different pathways involved inpathogenesis of diabetic neuropathy should be enhanced[6].

Currently, strict glycemic control and symptomatic relieve are the only modalities to treat diabetic neuropathy and still, the prevalence of this diabetic complication is rising. Dyslipidemia is an emerging factor involved in pathogenesis of diabetic neuropathy. So, this study contributes to the better understanding and knowledge of the lipid patterns in the patients with diabetes mellitus, suffering with peripheral neuropathy and patients with diabetes mellitus without neuropathy complications.

METHODOLOGY

This comparative-cross sectional study was carried out between January 2020 to September 2020 in Multidisciplinary Lab-1 of Biochemistry & Molecular Biology Department, Army Medical College in collaboration with Pak-Emirate Military Hospital, Rawalpindi. Research was conducted after formal approval of institutional ethics review committee.

Total eighty-four subjects were included in this study. Sample size was calculated using the World Health Organization (W.H.O) calculator based on reference prevalence (6.9%)[11], with 95% confidence interval and 5% error. The study participants were recruited by non-probability, consecutive sampling technique and divided into three groups. Group I included 28 patients with diagnosed type 2 diabetes mellitus with peripheral neuropathy, group II includes 28 patients with diagnosed type 2 diabetes mellitus without neuropathy and group III comprised of 28 healthy control subjects. These subjects were enrolled after taking informed consent and clinical and demographic data obtained using a structured questionnaire. Patients with and without diabetic

peripheral neuropathywere diagnosed by the medical specialists in PEMH Rawalpindi.

Patients with diabetic neuropathy and without diabetic neuropathy of both genders between the age group 30-70 years were included in the study and patients with non-diabetic neuropathy, pedal edema, lumbosacral pathology and limb amputations were excluded. Serum lipid profile included total cholesterol (TC), serum triglyceride (TAG), high-density lipoprotein cholesterol (HDL-C) and low-density lipoprotein cholesterol (LDL-C) was measured. Total 5 ml of fasting (8-12 hours fasting) venous sample wasdrawn from eachparticipant. Lipid profile parameters were measured by Siemens Advia automated chemistry analyzer.

SPSS-22 (statistical package for social sciences-22) was used for data analysis. Categorical variables were expressed as percentage while quantitative variables were assessed as mean ± standard deviation (± SD). One–way ANOVA test was used followed by post-Hoc Tukey test and *p*-value ≤0.05 was considered significant.

RESULTS

Total eighty-four subjects were enrolled in this study between the age-group of 30-70 years of both genders and divided into three groups. Among them there were 53 (63.1%) males and 31 (36.9%) females with mean age 50.75 ± 10.37years of participants. Group I included 18 (64.3%) males and 8 (35.7%) females, group II included 20 males (71.4%) and 8 (28.6%) females, while group III included 15 (53.6%) males and 13 (46.4%) females. The mean values of TC, TAG, HDL-C and LDL-C with ANOVAare given in table-I. Group comparison by ANOVA followed by post-Hoc Tukey test is given in table-II.

Table-I: Mean values of lipid profile of all groups.

Parameters	Group I (Diabetic with neuropathy) Mean ± SD	Group II (Diabetics without neuropathy) Mean ± SD	Group III (Healthy-controls) Mean ± SD	*p*-value
Total cholesterol (TC) mmol/L	4.87 ± 1.6	4.52 ± 0.72	4.23 ± 0.72	0.102
Triglycerides (TAG) mmol/L	2.75 ± 2.29	2.45 ± 0.94	1.31 ± 0.52	0.001*
High-density lipoprotein cholesterol (HDL-C) mmol/L	1.02± 0.22	0.99 ± 0.21	1.22 ± 0.22	<0.01*
Low-density lipoprotein cholesterol (LDL-C) mmol/L	3.07± 1.11	3.09 ± 0.64	2.81 ± 0.71	0.361

Table-II: Comparisons of the groups by anova followed by post hocks tuckey test.

Parameters	Group I v/s		Group II v/s
	Group II	Group III	Group III
Triglycerides (TAG)	0.714	0.001*	0.13
High-density lipoprotein cholesterol (HDL-C)	0.872	0.003*	0.001*
Total cholesterol (TC)	0.459	0.083	0.598
Low-density lipoprotein cholesterol (LDL-C)	0.995	0.461	0.405

The mean value of triglycerides was significant (<0.05) between group I and III and insignificant (0.714) between group I and II as well as (0.13) in group II and III. Triglycerides levels were higher in patients with diabetic neuropathy as compared to other groups. While the mean value of HDL-C was significant among group I and III as well as group II and III. Mean value of HDL-C was lowest in group II as compared to others. Mean value of total cholesterolwas high in group I as compared to group II and III, but that was not statistically significant. Similarly, mean value of LDL-C was higher in group II as compared to group I and III and it was non-significant. All parameters of lipid profile were statistically insignificant between group I and II.

DISCUSSION

Diabetic neuropathycauses malfunctioning of peripheral nerves which can progress to foot

ulceration, ultimately leading to limb amputation. The main focus of this study was to evaluate lipid profile in patients with diabetic neuropathy and without neuropathy. The key findings obtained in this study were the presence of significant difference in triglyceride and HDL-C levels among patients with diabetic neuropathy, without neuropathy and healthy controls. However, no significant statistical difference was found among diabetics with neuropathy and without neuropathy. Considering laboratory results, there was significant variation in HDL-C levels between diabetics without neuropathy and healthy controls. However, no statistically significant difference was found regarding triglyceride levels between these groups.

In concordance to our study, similar results were reported by Mohapatra & Damodar as they conducted the studyfor the evaluation of lipid profile and glycemic control among different stages of diabetic neuropathyand controls. They reported the significant reduction in HDL-C levels with increasing severity of diabetic neuropathy and increased triglyceride levels and increased LDL/HDL ratio were found in patients with diabetic neuropathyas compared to control[12]. Another study compare lipid profile parameters between patients with diabetic neuropathy and diabetics without neuropathy and reported the findings consisted to our study that non-significant reduction in HDL-C and elevation in triglyceride levels among these groups[13]. On the other hand, a study conducted by Pai *et al*, on Taiwanese population, in which association of lipid profile was analyzed in patients with diabetic peripheral neuropathy with or without neuropathic pain. This study showed significant association of high level of triglycerides in patients with diabetic neuropathy without pain as compared to diabetics without neuropathy, while lower levels of HDL-C were independently correlated patients with diabetic peripheral neuropathywith pain[14].

Deranged lipid profile is also associated with other microvascular complications. A study conducted on Pakistani population by Amin *et al*, for comparison of lipid profile in patients with diabetes mellitus with retinopathy and without retinopathy. They found consistent result to our study that significant increase in triglyceride levels and reduction in HDL-C levels in patients withdiabetic retinopathy as compared to controls. There was also strong positive association of serum LDL-C, total cholesterol and triglyceride with severity of diabetic retinopathy[15].

In this study, the mean value of total cholesterol was higher in patients with diabetic neuropathy as compared to other groups but was statistically not-significant. On the other hand, mean value of LDL-C was high in patients with diabetes mellitus without neuropathyas compared to other groups but it was also statistically non-significant. Lin *et al*, reported similar results that the high levels of total cholesterolin patients with diabetic neuropathy as compared to without neuropathy. But these findings were statistically significant in contrast to our study. A significant positive correlation between lipid profiles and HBA1c level was also observed in their study[16].

In contrast to these results, Jende *et al*, reported in their study that serum cholesterol and LDL-C levels were low and correlated with peripheral nerve swelling in patients with diabetic peripheral neuropathy. So, patients with diabetes mellitus on lipid lowering therapy and with very low cholesterol levels should be vigilant regarding onset or further-worsening of neuropathic symptoms[17]. Contradictory to our study, another study also found statistically significant decreased levels of total cholesterol in patients with diabetic neuropathy as compared to without diabetic neuropathyand statically significant decrease levels of triglyceride in patients with DPN as compared to without DPN[18]. One study reported the significant reduction in the levels of LDL-C and total cholesterol and these were correlated with increasing severity of DPN stages[12]. Herder *et al*, reported significant increase levels of total cholesterol (0.002) and LDL-C (0.005) in patients without DSPN as compared to patients with DSPN[19]. A systemic review and meta-analysis carried by Naqvi *et al*, to evaluate the predicting value of LDL-C levels in patients withand with-

out diabetic peripheral neuropathy. A significant correlation of reduced LDL-C with poor prognosis of DPN and diabetic foot was reported by them20. Aguiar *et al*, found significant association among total cholesterol and triglyceride levels and DPN. So, patients with diabetes mellitus having raised level of total cholesterol and triglyceride should be screened for neuropathy[21]. Increased levels of LDL-C were observationally and genetically correlated with increase risks of peripheral arterial disease and chronic kidney disease in a study conducted by Emanuelsson *et al*, and they also reported increased levels of LDL-C were not correlated with retinopathy and neuropathy in patients with diabetes mellitus[22].

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CONCLUSION

Serum triglyceride levels were significantly increased and high-density lipoprotein cholesterol levels were significantly decreased in patients with diabetic neuropathyas compared to healthy controls. There was no significant difference was observed regarding all lipid profile parameters between patients with diabetic neuropathy and without diabetic neuropathy.

CONFLICT OF INTEREST

This study has no conflict of interest to be declared by any author.

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