A COMPARATIVE STUDY OF DYSLIPIDAEMIA IN DIABETIC PATIENTS WITH AND WITHOUT NEUROPATHY

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ABSTRACT

Objective: To evaluate and compare lipid profile of diabetic neuropathic patients and diabetic patients without neuropathy.

Study Design: Cross-sectional comparative study.

Place and Duration of Study: The study was conducted at Multidisciplinary lab 1, Department of Biochemistry and Molecular biology Army Medical College, Rawalpindi in collaboration with department of Neurology PEMH Rawalpindi, from Feb 2018 to Sep 2018.

Material and Methods: The enrolled subjects were divided in to three groups, group I, n=30 healthy individuals taken as controls, group II composed of 30 diagnosed diabetic patients without neuropathy and group III comprised of 30 diagnosed diabetic patients with neuropathy.

Results: There was significant difference in HDL and LDL values between group I and group II. There was also significant difference in HDL and LDL values of group I and group III. There was no statistically significant difference of lipid profile parameters between group II and group III.

Conclusion: There was significant increase of LDL and decrease of HDL in diabetic patients as compared to normal healthy individuals. There was no statistically significant difference observed between the lipid profile of diabetics with and without neuropathy.

Keywords: Diabetes mellitus, Diabetic neuropathy, Dyslipidemia.

INTRODUCTION

Diabetes mellitus (DM) is a chronic systemic disorder characterized by increased glycemic levels, deranged lipid profile and high oxidative stress levels. Oxidative stress acts as the main spawn of diabetic complications[1]. The global Diabetic population is 366 million and is estimated to be doubled by the year 2030[2] while, the estimated prevalence in Pakistan is 11.7%[3]. One of the most alarming notions, by the international Diabetes Federation is that, about 7 million people of Pakistan were suffering from DM in 2015 and are predicted to rise up to 14 million by 2040[4]. Approximately 1.6 million deaths are caused directly by DM and its complications all around the world[5].

Prolonged hyperglycemia is considered as the main culprit leading to increased lipid peroxidation, oxidative stress that ultimately leads to acute and chronic diabetic complications. One of the more serious complications is Diabetic Neuropathy (DN) which is a debilitating microvascular complication and is present in roughly 50% of diabetics all around the world[6]. The prevalence of diabetic neuropathy is rising briskly in Asia: in Japan, 40%[7]; in China, 42.8%[8]; in Malaysia, 46%[9]; prevalence has been reported. In Pakistan the prevalence is about 30%[10]. DN itself is a neuro-degenerative disease that targets the peripheral nervous system, characterized by, pain, allodynia, hyperalgesia and paresthesia[11].

DPN is the most common cause of hospital admissions among diabetic complications and non-traumatic amputations[12]. The metabolic factors which are considered responsible for development of diabetic neuropathy are bad glycemic control, duration of diabetes, dyslipidemia, obesity and hypertension. Non metabolic

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strands like, age, genetic vulnerability, height, gender, smoking and alcohol consumption are also been considered as the probable risk factors for the neuropathy[13].

Dyslipidemia is common in type 2 diabetics[14], because of which it has been implicated as cause of microvascular complications[2]. The lipoprotein changes that are observed usually in type2 DM are hypertriglyceridemia, reduced HDL and raised LDL which is converted probably to smaller atherogenic lipoproteins[15]. Dyslipidemia leading to damage in the neural cell and the nerve tissues resulting in neural ischemia, which is a key characteristic in DN[16]. Nerve dysfunction leading to cell death in DN are the sequel of a complex myriad of events that are prompted by the metabolic disparity associated with diabetes[16]. The exact pathophysiology of DN is not known but, it is postulated that high levels of lipid in the nerve cell activate the poly (ADP-ribose) polymerase (PARP) pathway which in turn activates the AGE (advance glycation end products) pathway leading to excessive formation inflammatory cytokines[13]. The Hexosamine pathway also activates oxidative stress. Inflammatory cytokines and oxidative stress together results in neuronal cell dysfunction and death, which is manifested as DN.

Diabetes can be the cause of different types of neuropathy, the most common being the bilaterally symmetrical damage to the nerves of the feet, with severity gradient rising proximally, commonly known as stocking glove neuropathy[17]. Primarily diabetic neuropathy is the disorder of sensory nerves thus explaining the reason for pain, tingling, pricking sensations and numbness in the beginning followed much later by motor nerve dysfunction[17]. More neuropathies that can be seen in both type 1 DM and type 2 DM are autonomic neuropathy, polyradiculoplexus neuropathy, mono-neuropathies, cranial neuropathies, and treatment induced neuropathies[13].

Limited studies have been reported, in which different parameters of neuropathy are compared between diabetics and diabetics with neuropathy[6,18]. In this current study the lipid profile of diabetic patients is being compared with that of neuropathic diabetics.

MATERIAL AND METHODS

This cross-sectional comparative study was conducted at Multi disciplinary lab I in collaboration with department of Neurology PEMH Rawalpindi, from February 2018 to September 2018. Approval form the institutional ethical review committee was taken. Patients was included after taking informed consent. The sampling technique applied was non probability purposive sampling and the sample size was calculated by the WHO calculator based on 30% population proportion with 95% confidence interval and 10% precision[10].

Total of 90 individuals (both genders) between the ages of 40 to 70 years were included. They were divided into following three groups,

Group-I: Normal healthy controls (group I, n=30).

Group-II: Diagnosed diabetics without neuropathy (group-II, n=30).

Group-III: Diagnosed diabetics with neuropathy (group-III, n=30).

Non-diabetic neuropathic patients were excluded. Neuropathic diabetic patients were diagnosed by neuro-physician at neurology department at PEMH Rawalpindi. Clinical and demographic data was collected through a proforma. Fasting venous blood 5ml was drawn and stored in vacutainers. The measurement of serum total cholesterol (TC), TG and HDL were quantified by using commercial kits, in according to the instructions of the manufacturers. The data was entered and analyzed using SPSS version 22.0. The arithmetic mean and standard deviation of TC, TG, LDL and HDL were calculated. The statistical significance of difference among the groups was determined by applying one way ANOVA followed by Post-Hoc Tuckey's test. A *p*-value of less than or equal to 0.05 was considered statistically significant.

RESULTS

Total of 90 individuals were included in this study, from both genders [males 55 (61%) and 35

$(p<0.05)$, whereas the difference in LDL levels of group II and group III was not significant $(p>0.05)$. Mean value of HDL level was

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

	Group-I (Controls) Mean ± SD	Group II (Diabetics without DPN) Mean ± SD	Group III (Diabetics with DPN) Mean ± SD	Significance (*p*-value)
TC (mmol/L)	4.87 ± 0.32	4.75 ± 0.89	4.85 ± 1.08	0.815
HDL (mmol/L)	1.16 ± 0.32	1.00 ± 0.21	0.95 ± 0.18	0.003
LDL (mmol/L)	2.17 ± 0.38	2.85 ± 0.86	3.08 ± 1.02	0.001
TG (mmol/L)	2.63 ± 0.49	2.57 ± 1.14	2.74 ± 1.10	0.793

Table-II: Comparisons of *p*-values among the groups by ANOVA followed by post hocks tuckeys test.

Lipid Profile	Group I - VS		Group II - VS
	Group II	Group III	Group III
HDL(mmol/L)	0.036	0.003	0.660
LDL(mmol/L)	0.004	<0.001	0.484

(39%) females] between the ages of 40 to 70 years were divided in three groups. The mean age of group I was 50.23 ± 6.44 years including 17 (56.7%) males and 13 (43.3%) females, group II

significantly higher in control group $(p<0.05)$ as compared to group II and group III, yet no significant difference was observed between group II and group III $(p>0.05)$. The mean value
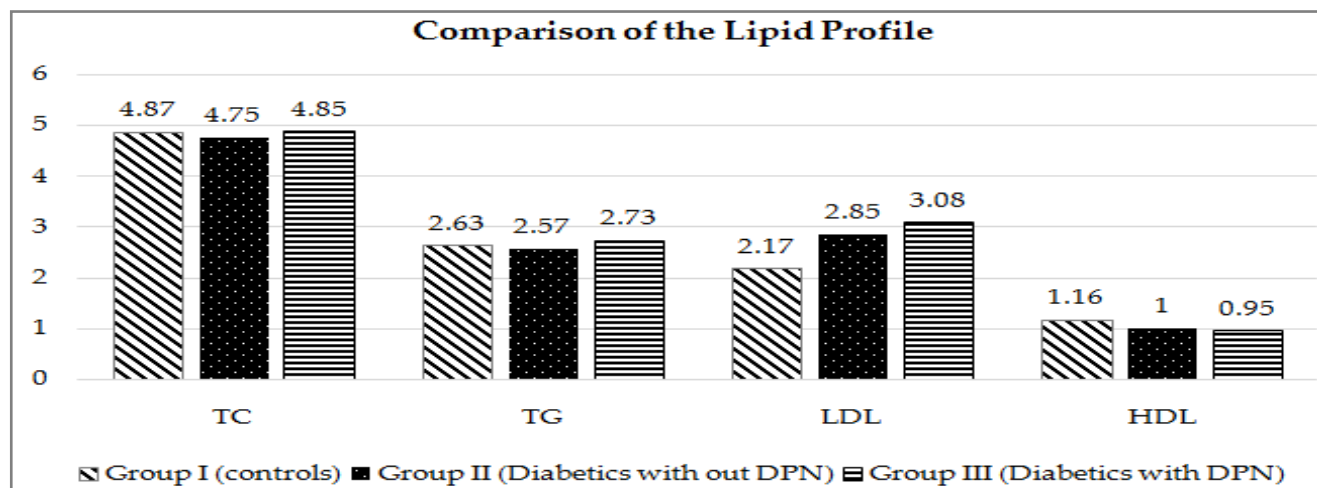

Figure: Comparison of the lipid profile among groups I, II, and III.

with the mean age of 51.53 ± 7.8 years including 20 (66.7%) males and 10 (33.3%) females, and finally group III with the mean age of 58.57 ± 8.94 years including 21 (70%) males and 9 (30%) females. Mean levels of TC, LDL, HDL and TGs for group I, group II and group III are mentioned in table-I. LDL level was significantly higher in group II and group III as compared to group I

of TGs is highest in group III but it is statistically in significant (table-II).

DISCUSSION

Diabetes mellitus is a vicious circle of insulin resistance or insulin deficiency, dyslipidemia and hyperglycemia, that leads to the development of diabetic microvascular and macro-vascular

complications including neuropathy, nephropathy, retinopathy, coronary artery diseases and cerebrovascular accidents; Among these foremost is the least studied and diagnosed[19]. Limited studies have been documented showing the comparison of diabetics without neuropathy and diabetics with neuropathy enhancing the need of this study.

In the current study, significant difference was observed in the levels of LDL and HDL among healthy controls, diabetics without neuropathy and diabetic neuropathic patients. No statistically significant difference was found between the diabetics and diabetics with DN. In a study by Jagannadha *et al* (2016), part of deranged lipid profile in pathogenesis of diabetic retinopathy was determined by comparing the diabetics with retinopathy, diabetics without retinopathy and healthy individuals as controls, they found the raised mean levels of total cholesterol, triglyecrides in diabetic patients with retinopathy as compare to diabteics without retinopathy but the difference among groups was not statistically significant[20]. On the other hand, in another study conducted on Chinese population by Song *et al* (2015), in which association of lipid profile was analyzed with diabetic cardiac autonomic neuropathy (DCAN), shows positive significant and independent association between TG and DCAN[14].

Our results are in concordance with the results of the study conducted by Kumar *et al*, in which lipid profile of type2 diabetic patients suffering from sensory neural deficit and non-diabetic controls were compared, their results depicted higher levels of TC, LDL and lower HDL levels in diabetic group as compared to control group hitherto the difference is there but not statistically significant[21]. Microvascular complications in newly diagnosed type 2 diabetics and its association with correlates of metabolic syndrome, a study conducted by Nikhitha *et al* (2017), there results showed no significant association between dyslipidemia and any micro vascular complications[12].

A recent research by Aneela *et al* carried out at biochemistry department, National University of Medical Sciences (NUMS) Rawalpindi compared the diabetics with retinopathy with healthy controls, found significant association with TC, TG, and LDL, while no significant association was observed with HDL[2].

In this study, the mean cholesterol levels in the control group was found to be non-significant higher than diabetic group, which may be attributable to the use of statins and other lipid lowering drugs in the diabetics with and without neuropathy, rather than healthy control which normally take no medication. Patricia *et al* in their study evaluated the effect of total cholesterol, triglycerides levels and statin use on clinical score of neuropathy in diabetic patients. In their study no significant relationship was found between DN and cholesterol or triglyceride levels[22].

Holmes *et al* (2015) conducted a study on rat models, diabetes and dyslipidemia was diet-induced, they concluded that weight loss and low fat diet was not sufficient to improve peripheral neuropathy deficits, once hyperglycemia was developed[23].

CONCLUSION

There was significant increase of LDL and decrease of HDL in diabetic patients as compared to normal healthy individuals. There was no statistically significant difference observed between the lipid profile of diabetics with and without neuropathy.

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CONFLICT OF INTEREST

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

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