

Deranged Haematological Profile and Dyslipidaemia in Diabetes Induced Nephropathy

Abstract

Background: Diabetic nephropathy caused by complication of diabetes mellitus and frequently increasing in the developed countries. It may be characterized by dyslipidaemia and deranged haematological indices that play a role in the development of late complications of diabetes. Therefore, there is an urgent need to develop strategies to diagnose the patients of diabetic nephropathy during its acute phase.

Objective: To determine the haematological indices and the lipid profiles in diabetic nephropathy in comparison with diabetic controls

Methodology: The present study was performed on total of 300 patients where 150 DN patients and 150 control with age range from 30-50 years. The haematological profile was done via ABX Micros 60 haematology analyser, analysis of lipids, fats and fatty substances lipid panel was also performed in both groups. Statistical analysis was done with SPSS through t-test where $p \geq 0.05$.

Results: Current data indicated that the level of Haemoglobin A1c, Prothrombin time, White blood cells, platelet count, Low density lipoproteins and triglyceride is raised while significant reductions in red blood cell count and high-density lipoprotein levels have been noted in patients with diabetic nephropathy compared to diabetics.

Conclusion: Our research indicates that both haematological and lipid profiles are highly disturbed in DN patients which may serve as a hallmark for early diagnosis of nephropathy in diabetics.

Keywords: *Diabetic nephropathy (DN), End-stage renal disease (ESRD), Diabetes mellitus (DM), LDL, HDL.*

1. INTRODUCTION

The prevalence of diabetes is increasing worldwide, within ethnic and racial groups of Asia and Africa at greater risk [1]. The number of people with diabetes has increased due to an urbanization, aging, and reduced level of physical activity. Poorly controlled diabetes can lead to various problems such as nephropathy, neuropathy retinopathy, and oxidative stress leading

damage to tissues and cells [2, 3]. The total time of exposure to hyperglycemia is responsible for the complications and adverse outcomes of DM [4].

Diabetic nephropathy (DN) is recognized the most important microvascular complications of diabetes mellitus (DM) and has become the single most common cause of end-stage renal disease (ESRD) worldwide [5], traditionally defined as the gradual rise in albumin with blood pressure. Elevated and excreted, resulting in decreased glomerular filtration and ultimately ESRD. The disease is also characterized by morphological and functional changes in the kidneys, such as glomerular hyperfiltration, glomerular and renal hypertrophy, increased urinary albumin excretion, increased basement membrane thickness, and meningeal dilatation, accompanied by extracellular matrix proteins (accumulation of proteins such as laminin collagen and fibronectin) [6-8] leads to severe dysregulation of some enzymes and metabolic pathways in diabetic nephropathy; this ultimately leads to high-density lipoprotein (HDL), cholesterol, and Lipoprotein levels of triglycerides are disturbed [9]. High levels of total and non-HDL cholesterol, as well as low levels of HDL cholesterol, were significantly associated with an increased risk of kidney dysfunction in healthy individuals. Carbohydrate metabolism directly affects lipid profile in diabetes. Also insulin deficiency may influence the level of free fatty acid. Abnormalities in lipid profile also play an essential role in vascular risk associated with type-2 DM [10, 11].

The aim of this study was to evaluate hematological parameters and lipid profiles in patients with diabetic nephropathy. This study aims to raise awareness of the need for hematology and lipid analysis in patients with diabetic nephropathy so that the necessary actions can be taken to optimize their management early and prevent late complications.

2. METHODOLOGY

2.1. Study Design, Period and Area

The study was a case control (retrospective) study which was conducted between January to December 2018. The present research work was conducted at Institute of Molecular Biology and Biotechnology, The University of Lahore, Lahore, Pakistan

2.2. Study Participants

Total number of patients was three hundred (300) out of them one hundred and fifty (150) patients of diabetic nephropathy with the age group of 30-50 years and One hundred and fifty age-matched diabetic controls without nephropathy (150) included in the current study. All the

patients suffering from diabetic nephropathy with the confirmed clinical reports were recruited. The patients with the history of smoking, metabolic dysfunction, malnutrition, on statins for abnormal lipid treatment, on anticoagulant therapy and who had chronic diseases were excluded from the study.

2.3.Sampling Technique

Convenient non-probability sampling technique was employed to select the study participants.

2.4.Ethical Consideration

Ethical clearance was obtained from the “Research and Ethics Committee” at Institute of Molecular Biology and Biotechnology, The University of Lahore, Lahore, Pakistan. An informed consent from every patient was taken before the start of research work.

2.5.Data Collection and Laboratory Methods

Five ml of venous blood was drawn from patients of diabetic nephropathy and control individuals. Then the sample was centrifuged within two hours at 3000 rpm. After the centrifugation, the serum was separated and stored at -70°C for the examination. The sample was transferred in the laboratory for further processing.

2.6.Haematology profile

Complete blood count comprising red blood cell count, white blood cell count and differentials, and platelets were determined from the remaining whole blood that was placed in EDTA test tubes using ABX Micros 60 Haematology Analyser (Horiba-ABX, Montpellier, France).

Estimation of HBA1C is done by high performance liquid chromatography. HBA1C values are expressed as percentage i.e <7% is considered normal. Prothrombin time was estimated by Quick’s method [26].

The biochemical measurements made were triglycerides, total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), and low-density lipoprotein cholesterol (LDL-C) levels in blood by spectrophotometric method and enzymatic method [26].

2.7. Statistical Analysis

Data was analysed using Statistical Package for Social Sciences (SPSS, Version 17.0). Normally distributed data was analysed using T-test. A p-value of < 0.05 was considered statistically significant.

3. RESULTS

3.1. Demographic and Clinical Characteristics of Study Group

A total of 300 (150 diabetic control, 150 diabetic nephropathy) participants were included in this study. The mean age of DN patients was 45.61 ± 17.89 yrs and mean age of healthy group was 42.85 ± 5.15 yrs. The mean weight and BMI of nephropathy patients group were 51.61 ± 11.50 kg and 25.4 ± 3.2 kg/m² respectively, as compared to normal subjects' 41.22 ± 2.25 kg and 23.2 ± 3.2 kg/m², respectively.

The mean systolic and diastolic blood pressure in patients suffering from diabetic nephropathy was recorded to be 130.33 ± 6.75 mmHg and 80.75 ± 2.27 mmHg, respectively, while in the control group mean systolic and diastolic BP values of 121.91 ± 2.24 mmHg and 78.56 ± 1.19 mmHg, respectively, were observed (Figure 1).

3.2. Hematological Profile

The mean value of Red Blood Cells (RBCs) in the control group was 6.58 ± 2.88 μ g/dl and in the DN group was 4.59 ± 1.45 μ g/dl. The mean White Blood Cells (WBCs) were 6.59 ± 1.59 ($\times 10^9$ /L) and 8.59 ± 2.48 ($\times 10^9$ /L) in the control group and DN group, respectively. There was a significant raise in WBCs in the study subjects. It was also found that platelets were increased by $255.7 \pm 82.0 \times 10^3/\mu$ l in the DN group compared with $246.3 \pm 67.4 \times 10^3/\mu$ l in the control group. A poor glycemic control was observed in the DN group indicated by HbA1C value of 9.55 ± 3.01 as compared to the controls 7.59 ± 1.77 . The mean prothrombin time determined in DN patients was increased (16 seconds) compared to the control group (13 seconds) (Figure 2).

3.3. Lipid Profile

Mean total cholesterol and triglycerides were significantly increased in the patients with diabetic nephropathy (5.2 ± 1.2 mmol/L and 2.58 ± 1.43 mmol/L) as compared to healthy individuals (4.92 ± 0.97 mmol/L and 2.27 ± 1.0 mmol/L), respectively. An elevated trend of LDL was found in diseased group (3.2 ± 1.2 mmol/L) in comparison with control group (1.1 ± 5.5 mmol/L). However, the mean value of HDL was considerably decreased in the patients with diabetic nephropathy (1.8 ± 0.7 mmol/L) as compared to healthy control (3.5 ± 1.2 mmol/L) (Figure 3).

4. DISCUSSION

Diabetic nephropathy is characterized by uncontrolled secretion of urine albumin, loss of glomerular filtration rate and glomerular lesions. Different epidemiological studies determine that family history ethnicity, abnormal haematological profile, gestational diabetes, elevated blood pressure, dyslipidaemia and obesity are the major risk factors of diabetic nephropathy[12] Other putative risk factors include external environmental pressure such as

smoking and inhalation of other toxins, elevated glycosylated haemoglobin level (HbA1c), proteinuria and elevated systolic pressure [13]. Similar trend could be seen in the present study in which the levels of HbA1c, PLTs and WBCs were increased among the patients.

The literature suggests that in case of early detection of Diabetes among the patients it is necessary to estimate the haematological profile and detect the changes in comparison to the controls. In the present study, white blood cells, Platelets and HbA1c were remarkably higher in the study group, consistent with many other reported studies. Literature signifies that the raised levels of the haematological variables are the reason for inflammation, thrombosis, and coagulation among patients. A study by Adane *et al.*, in 2021 indicated that the White blood cells and platelets were higher in patients with Diabetes compared to the controls[14] Another similar study conducted in 2015 by Biadgo *et al.*, indicated an increasing trend in both the white blood cells and platelets among the diabetics [15]. A systematic review and meta-analysis of cross-sectional and prospective studies has shown that peripheral white blood cell counts such as basophils, eosinophils, and neutrophils increased without changes in monocyte counts in patients with diabetic nephropathy [16]. In addition, a study suggests that high platelet activity increases vascular complications in DM patients and that altered platelet morphology and function may be reflected as a risk factor for platelet reactivation in patients with diabetes [17]. The results of these studies coincide with the present study results. Another study observed that diabetics are prone to anemia due to impaired kidney function and reduced production of the hormone erythropoietin, which ultimately leads to reduced red blood cell counts.

Said and Hernandez pointed out in 2014 that increase in HbA1C was associated with increase in chronic kidney disease which supports the present study's raised percentage of HbA1C [18]. A study in 2015 in CKD cohort indicated that HbA1C prediabetes values are associated with higher mortality rates among the patients [19]. Another study by Lee *et al.*, in 2020 suggested that variation in HbA1C levels is considered as an independent risk factor for decreased kidney function in patients with type 2 diabetes [20] These studies, results are in accordance with the present study.

Many factors are known to affect lipid levels in diabetes, as carbohydrate metabolism directly affects lipid metabolism [21, 22]. There have been a number of studies showing that lipid abnormalities are associated with a reduction in kidney function in the general population. It is uncertain whether it is the lipid abnormalities that cause the reduction in kidney function or

whether impaired renal function or proteinuria itself causes both the lipid abnormalities and the reduction in renal function. The current study showed that levels of low-density lipoproteins (LDL) and triglycerides (TG) were increased and levels of high-density lipoproteins (HDL) were decreased in patients with diabetic nephropathy. In a study by Srinidhi Rai *et al.*, it was pointed out that the values of TG and LDL were significantly higher in type 2 diabetes with nephropathy compared to the controls [23]. A study measured plasma TG and HDL levels as predictors of development of diabetic kidney disease in 2016. It was seen that diabetic Dyslipidemia with high TG and low HDL levels is an important risk factor for developing diabetic kidney disease over a 4-year period [24]. Kachawa *et al.* emphasised that Dyslipidemia is a leading cause of chronic kidney disease in DN. Hence, lipids represent a useful clinical parameter for assessing renal disease progression in DN [25]. All these studies strengthen the results of the present study in terms of lipid derangements seen in DN patients compared to the controls.

5. CONCLUSION

We observed severe derangements in haematological parameters and lipid metabolism in patients with diabetic nephropathy. Our study showed that the levels of White blood cells, Platelets and HbA1C were significantly increased in diabetic nephropathy compared to healthy controls. This is an important risk factor for various cardiovascular and cerebrovascular diseases that can be detected with less expensive and simple blood tests in diabetics. Routine screening of deranged blood indices is recommended to decrease complications associated with diabetes. Also our study indicated severe dyslipidemia associated with DN patients. Elevated LDL, triglycerides, and decreased HDL levels also indicate an increased risk of atherosclerotic disease in diabetics. Therefore, lipid profiling can provide a useful clinical tool not only to identify patients at higher risk for kidney disease, but also to assess the development and progression of kidney disease. The limitation of this study is that it does not assess a cause-and-effect relationship between variables and patients with diabetic nephropathy.

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CONFLICT OF INTEREST

Authors declare no conflict of interest

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

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Figure legends

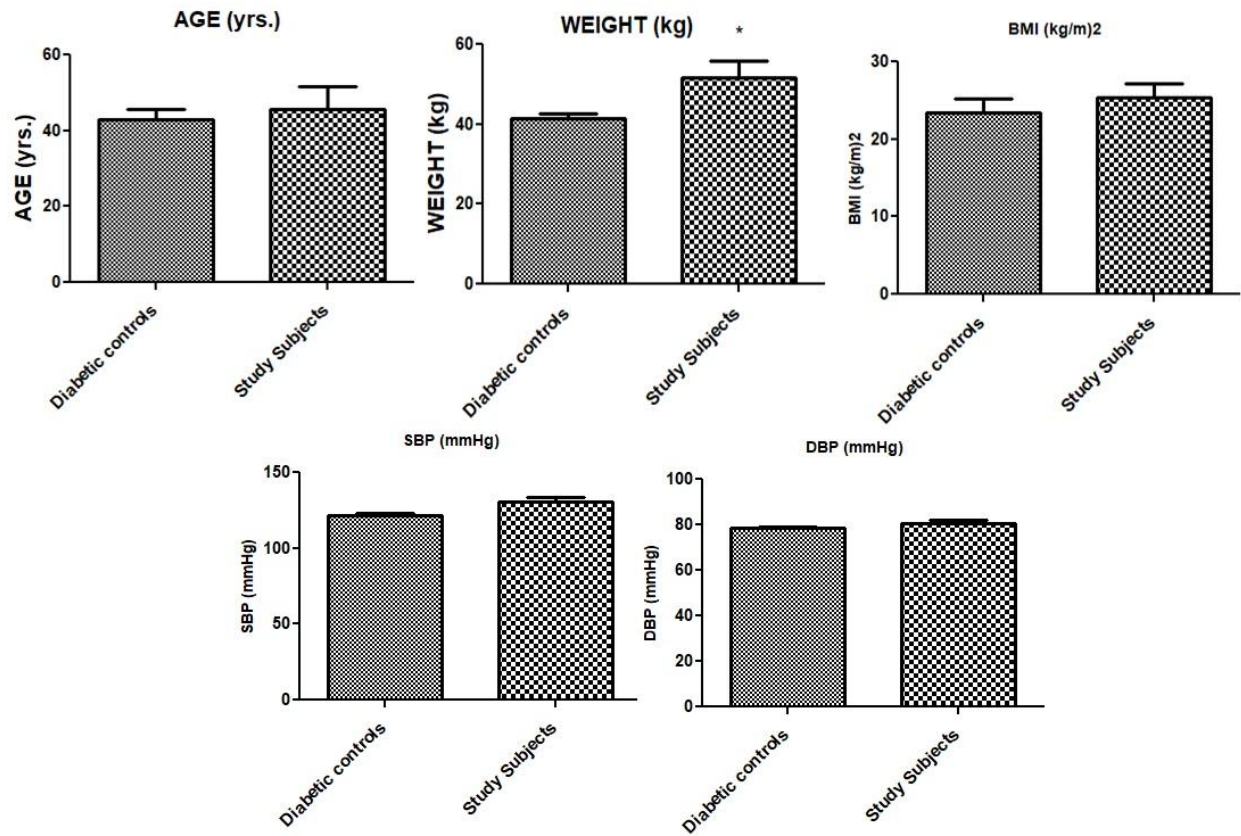


Figure 1: Demographic and clinical variables in diabetic nephropathy

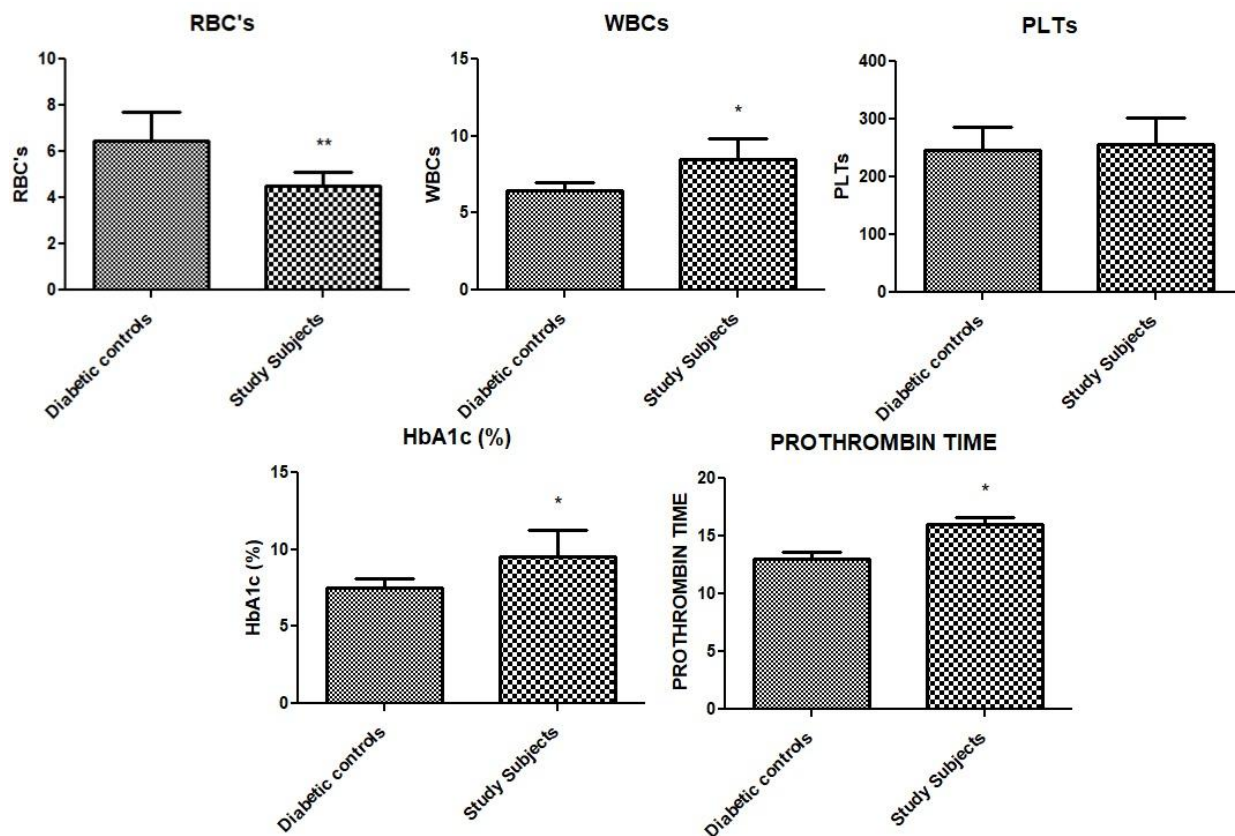


Figure 2: Comparison of heamatological indices of the study participants

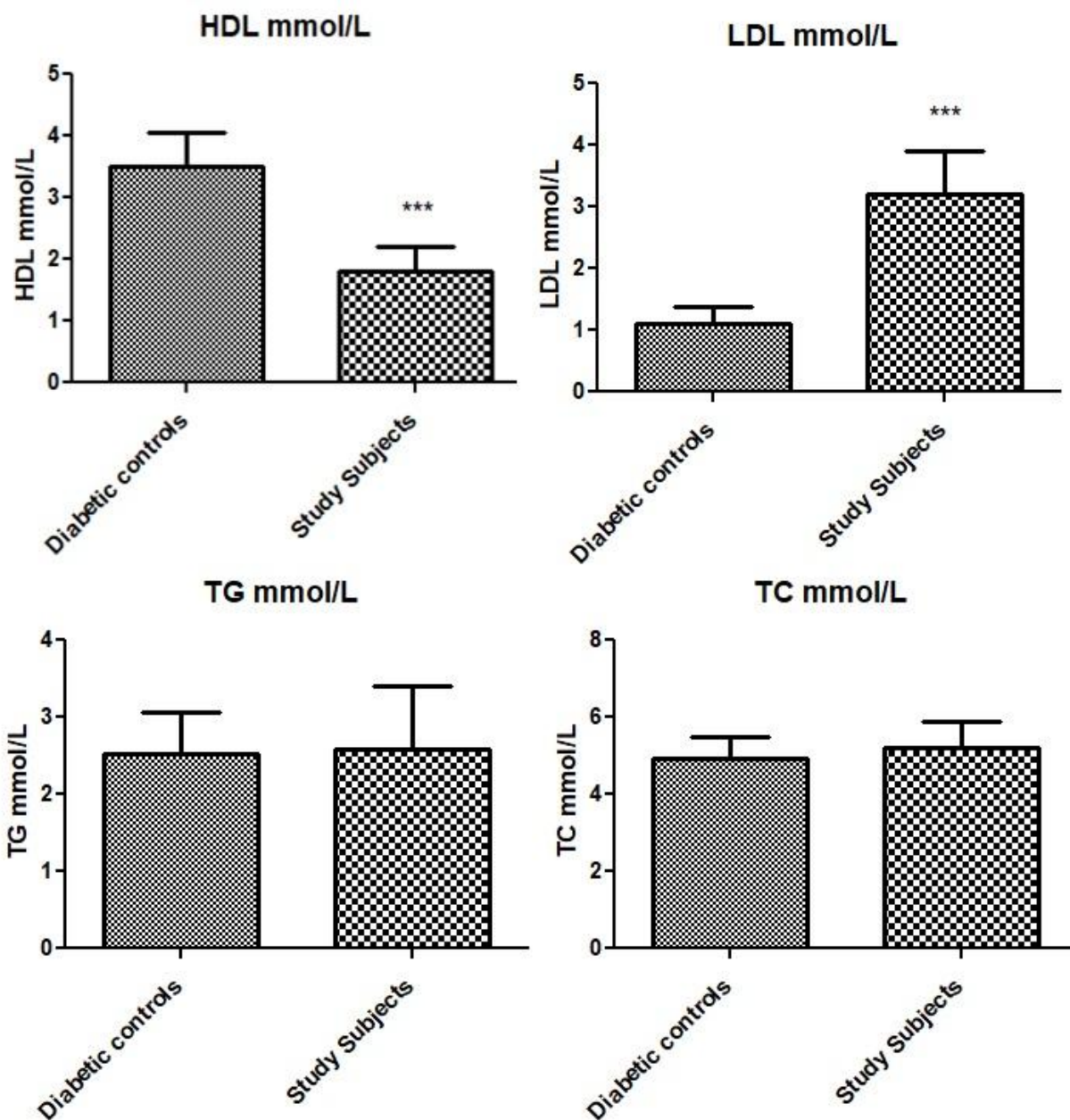


Figure 3: Lipid profile of diabetic control and patients of diabetic nephropathy