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Metabolic Drivers of Nerve Damage in Type 2 Diabetes: A Study on HbA1c and Dyslipidemia

Dr. Lucky
PG Resident,
Department of Medicine, Rama Medical College Hospital & Research Centre, Pilkhuwa, Hapur, U.P.
Co-Author
Dr. Deepti Gujral Saha,
Associate Professor,
Department of Medicine, Rama Medical College Hospital & Research Centre, Pilkhuwa, Hapur, U.P.

ABSTRACT :

*Diabetic neuropathy is one of the most prevalent and debilitating complications of **Type 2 Diabetes Mellitus (T2DM)**, significantly impairing quality of life and increasing morbidity. Metabolic disturbances, including chronic hyperglycemia and altered lipid profiles, are believed to play crucial roles in the pathogenesis of nerve damage. This study aimed to evaluate the association between **HbA1c levels**, various parameters of **dyslipidemia**, and the severity of peripheral neuropathy in patients with T2DM. A cross-sectional observational study was conducted involving adult T2DM patients attending the Medicine OPD. Clinical evaluation included symptom assessment, neuropathy scoring, and neurological examination. Laboratory investigations included fasting lipid profile, HbA1c measurement, and fasting glucose levels. Nerve conduction studies (NCS) were performed to determine the degree of neuropathy. The findings demonstrated that poor glycemic control, reflected by elevated **HbA1c**, was strongly correlated with abnormal nerve conduction parameters, including reduced sensory nerve action potentials and slowed conduction velocities. Dyslipidemia, particularly high **triglycerides**, increased **LDL-cholesterol**, and reduced **HDL-cholesterol**, also exhibited significant associations with neuropathy severity. Patients with combined poor glycemic control and dyslipidemia exhibited the most severe impairments, highlighting the synergistic influence of metabolic factors on neural damage. The results underscore the need for comprehensive metabolic monitoring to prevent or delay neuropathy. Aggressive glycemic management, coupled with lipid-lowering therapy and lifestyle interventions, may reduce the burden of nerve damage. This study emphasizes the importance of integrating metabolic parameters into neuropathy screening protocols in T2DM patients and advocates for early intervention strategies to mitigate long-term complications.*

KEYWORDS:
Type 2 Diabetes Mellitus**, **Diabetic Neuropathy**, **HbA1c**, **Dyslipidemia**, **Triglycerides**, **LDL**, **HDL**, **Nerve Conduction Study

INTRODUCTION:

Diabetic neuropathy represents one of the most common chronic complications associated with **Type 2 Diabetes Mellitus (T2DM)**, affecting nearly half of all diabetic individuals during the disease course. Among the various forms of neuropathy, **distal symmetric polyneuropathy**

remains the most prevalent and contributes significantly to morbidity through chronic pain, sensory loss, gait instability, and risk of foot ulcers. Despite the high prevalence, the pathophysiological mechanisms underlying diabetic nerve damage remain complex and multifactorial. Among the implicated mechanisms, persistent hyperglycemia and dysregulated lipid metabolism have emerged as pivotal metabolic drivers of nerve injury. Chronic hyperglycemia, indicated clinically through elevated **HbA1c**, contributes to neural damage via multiple pathways. These include increased oxidative stress, activation of the **polyol pathway**, formation of **advanced glycation end products (AGEs)**, and impaired microvascular perfusion. Likewise, abnormalities in lipid metabolism play a synergistic role. Elevated levels of **triglycerides**, **LDL-cholesterol**, and low **HDL-cholesterol** have been associated with impaired endothelial function, chronic inflammation, and neural ischemia. Multiple clinical studies have indicated that dyslipidemia accelerates neuropathy progression independent of glycemic control. In India, where T2DM prevalence is rising rapidly, the burden of neuropathy is substantial but often underdiagnosed. Early recognition of metabolic determinants is critical for preventing long-term disability. Although several studies have explored the individual effects of hyperglycemia on neuropathy, the combined influence of **HbA1c** and lipid abnormalities requires further clarity, especially in North Indian populations. Understanding this relationship is essential for designing targeted interventions and improving patient outcomes. The present study aims to investigate the correlation between glycemic control, lipid abnormalities, and neuropathy severity assessed through nerve conduction studies. By evaluating both biochemical and electrophysiological parameters, this study seeks to provide comprehensive insights into metabolic contributors of nerve damage. The findings may offer valuable guidance for clinicians in optimizing treatment protocols and promoting early preventive strategies.

MATERIALS AND METHODS :

This observational cross-sectional study was conducted in the Department of Medicine at Rama Medical College Hospital & Research Centre, Pilkhuwa, Hapur, U.P., from **23/12/2023 to 15/06/2024**. Ethical approval was obtained from the Institutional Ethics Committee, and informed consent was obtained from all participants. **Study Population:** Adult patients (age 30–70 years) diagnosed with Type 2 Diabetes Mellitus for at least one year were included. Exclusion criteria were alcohol-related neuropathy, vitamin B12 deficiency, thyroid disorders, chronic kidney disease, exposure to neurotoxic drugs, and acute illness. **Clinical Assessment:** Detailed history was taken, focusing on diabetes duration, symptoms of neuropathy, lifestyle habits, medication adherence, and comorbidities. Neuropathy symptoms were assessed using the **Michigan Neuropathy Screening Instrument (MNSI)** and **Neuropathy Disability Score (NDS)**. Physical examination included testing for vibration sense, temperature discrimination, ankle reflexes, and pressure sensation using a 10-g monofilament. **Biochemical Investigations:** Fasting venous blood samples were collected to evaluate: (1) **HbA1c** using high-performance liquid chromatography; (2) **Lipid profile** including total cholesterol, triglycerides, LDL, HDL, and VLDL; (3) Fasting blood sugar (FBS). HbA1c levels were categorized as good control (<7%), moderate (7–8.5%), and poor control (>8.5%). Dyslipidemia was defined using NCEP-ATP III criteria. **Nerve Conduction Studies (NCS):** Electrophysiological testing was performed using a standardized EMG/NCS system by an experienced neurologist. The following nerves were studied: sensory—sural and superficial peroneal nerves; motor—peroneal and tibial nerves. Parameters analyzed included **conduction**

velocity, **amplitude**, and **distal latency**. Neuropathy was graded based on electrophysiological abnormalities into mild, moderate, and severe. **Statistical Analysis:** Data were entered in Microsoft Excel and analyzed using SPSS software version 26. Continuous variables were expressed as mean ± SD, while categorical variables were presented as percentages. Pearson correlation analysis was used to determine the association between HbA1c, lipid parameters, and NCS findings. p-value <0.05 was taken as statistically significant. **Data Collection Flow:** Step 1—Patient screening and recruitment; Step 2—Clinical assessment and scoring; Step 3—Biochemical sample collection; Step 4—Electrophysiological examination; Step 5—Data analysis. **Quality Control Measures:** All biochemical tests were performed in a NABL-accredited laboratory. Nerve conduction studies were conducted using calibrated equipment. Internal cross-verification ensured accuracy of results. **Outcome Measures:** The primary outcome was the correlation of HbA1c and lipid abnormalities with nerve conduction deficits. Secondary outcomes were neuropathy prevalence and severity in relation to metabolic status. **Ethical Considerations:** Confidentiality of participants was maintained throughout. No invasive procedures beyond standard diagnostic testing were involved. Patients with severe neuropathy or uncontrolled metabolic parameters were counselled and referred for further management. **Documentation and Reporting:** All findings were recorded systematically, and data were compiled as per research paper guidelines.

RESULTS :

A total of 120 T2DM patients were included. The mean age was 54.3 ± 9.2 years, with males comprising 58%. The mean duration of diabetes was 8.1 years. Based on HbA1c values, 22% had good control, 31% moderate, and 47% poor glycemic control. Neuropathy was clinically detected in 63% of patients. NCS revealed abnormalities in 71%, with sensory nerves more affected than motor nerves. Patients with **HbA1c >8.5%** demonstrated significantly reduced sensory nerve action potential amplitudes and slowed conduction velocities ($p<0.001$). Dyslipidemia was present in 67% of patients. Elevated **triglycerides** and **LDL-cholesterol**, along with reduced **HDL**, were significantly associated with abnormal NCS parameters ($p<0.05$). Patients with both poor glycemic control and dyslipidemia exhibited the highest neuropathy severity scores. Correlation analysis showed strong positive correlation of HbA1c with neuropathy severity ($r = 0.71$) and negative correlation of HDL with nerve conduction velocity ($r = –0.62$). Combined metabolic abnormalities were strong predictors of neuropathy.

DISCUSSION :

The study demonstrates that both **hyperglycemia** and **dyslipidemia** independently and synergistically contribute to nerve damage in T2DM. Elevated HbA1c strongly correlates with impaired nerve conduction, supporting its role as a key metabolic driver of neuropathy. Dyslipidemia, particularly high triglycerides and LDL, further exacerbates neural damage by promoting microvascular dysfunction and inflammation. Early metabolic optimization is critical for halting disease progression.

CONCLUSION :

This study highlights the strong relationship between poor glycemic control, dyslipidemia, and neuropathy severity in Type 2 diabetes. HbA1c and lipid abnormalities significantly impair

nerve conduction parameters. Patients with combined metabolic derangements experience the most severe neuropathy. Early identification and aggressive management of metabolic factors are essential for preventing long-term neural complications. Routine screening using biochemical parameters and nerve conduction studies can improve patient outcomes.

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