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ORIGINAL ARTICLE

Prevalence of peripheral neuropathy in pre diabetic patients presenting to endocrinology department of DHQ Hospital Bannu.

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ABSTRACT… Objective: To determine the prevalence of peripheral neuropathy in pre-diabetic patients. **Study Design:** Cross-sectional, Observational. **Setting:** Endocrinology Department DHQ Hospital Bannu. **Period:** 11th April 2025 to 11th July 2025. **Methods:** A total of 132 pre-diabetic patients (HbA1c 5.7-6.4%) were studied using a non-probability consecutive sampling method. Peripheral neuropathy was diagnosed in these patients by endocrinologist through standard clinical neurological examination using 128Hz tuning fork (vibration, proprioception), tendon reflex testing and 10gm monofilament (touch sensation). **Results:** Out of 132 prediabetic patients, 48 (36.4%) reported neuropathic symptoms only (mostly burning sensations), while 69 (52.3%) were asymptomatic. Symptoms duration mostly ranged from 1 to 6 months. However, only 15 patients (11.4%) had both positive symptoms and positive signs of Peripheral neuropathy. **Conclusion:** Prediabetic patients frequently report neuropathic symptoms especially burning sensations, but clinical signs of peripheral neuropathy are less common. Early detection of neuropathy in prediabetic patients may prevent irreversible nerve damage in future.

Key words: HbA1c, Microvascular Complications, Prediabetes, Peripheral Neuropathy.

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INTRODUCTION

Diabetes is a chronic disease characterized by prolonged hyperglycemia. The complications of hyperglycemia are separated into macrovascular complications which include coronary artery disease, peripheral arterial disease, and stroke) and microvascular complications like diabetic nephropathy, neuropathy, and retinopathy.[1] Diabetic neuropathy, a common complication of diabetes involves progressive nerve damage that typically starts in the lower limbs, leading to sensory loss and chronic pain. Studies indicate that approximately half of all diabetic patients (50%) eventually develop neuropathy.[2] Pre-diabetes an intermediate hyperglycemic condition is a high-risk state for diabetes and is defined as glycemic variables that are higher than normal, but lower than diabetes thresholds. There is an enormous global burden of pre-diabetes, currently estimated to affect 374 million people worldwide and projected to increase to 548 million (8.6% of the global adult population) by 2045.[3] Research shows that individuals in the pre diabetic stage also experience diabetic complications affecting both the microvascular and macrovascular systems.[4] A systematic review that was conducted recently, including 29 studies (9351 participants) aimed to determine the prevalence of peripheral neuropathy in adults with pre-diabetes and to evaluate how prevalence estimates are influenced by the method of neuropathy assessment. Prevalence estimates varied widely from 2% (95% CI: 0%–4%) in a study conducted in the USA in women to 77% (95% CI: 54%–100%) in a study conducted in Brazil. The majority of studies (21 of 29, 72%) reported prevalence estimates ≥10%, primarily based on small nerve fiber tests.[5] There is now major interest in pre-diabetes and the closely related metabolic syndrome which is highly prevalent and enhances the risk of diabetes and macro vascular disease, but significant controversy exists in terms of peripheral neuropathy existence in prediabetic population.[6]

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According to a study conducted in Augsburg Germany a sample of 426 individuals aged 25–74 years from the KORA was examined to determine the prevalence of neuropathic pain across different glucose tolerance groups. The sample included 214 individuals with diabetes and 212 controls, which were further classified based on oral glucose tolerance test results into impaired glucose tolerance (IGT), impaired fasting glucose (IFG), and normal glucose tolerance (NGT). IGT and IFG groups were considered pre-diabetic. Neuropathic pain was identified using the Michigan Neuropathy Screening Instrument (MNSI), based on pain-related questions and an examination score with a cut-off point greater than 2. Diabetic individuals showed the highest prevalence of neuropathic pain (21.0%), followed by those with IGT (14.8% – pre-diabetes), IFG (5.7% – pre-diabetes), and lowest in those with NGT (3.7%) ($p < 0.001$).[7]

Between 25% and 62% of patients with idiopathic peripheral neuropathy are reported to have pre-diabetes, and among individuals with pre-diabetes 11–25% are thought to have peripheral neuropathy, and 13–21% have neuropathic pain.[8]

Objectives of the present study was to compare the prevalence of diabetic symmetrical peripheral neuropathy in pre-diabetic patients in our studied population with the worldwide available literatures and its correlation with life style, body mass index and other comorbidities.

METHODS

This cross-sectional study was conducted at department of Endocrinology DHQ hospital Bannu over a period of three months from 11th April 2025 till 11th July 2025 after approval of ethical committee (1871/Research/DHQ/BNU). Patients were selected with the help of pre-defined sample selection criteria. Patients diagnosed with pre-diabetes based on HbA1c 5.7 to 6.4% (ADA) based on test results from Shifa Laboratory. Patients having HbA1c level less or more than 5.7 to 6.4% or patients who use certain medications that cause neuropathy like on chemotherapy or on anti-HIV medication etc and female patients having gestational diabetic mellitus are excluded from the study. Only those patients were taken into study that fulfills the inclusion criteria and were agree to participate and sign questionnaire.

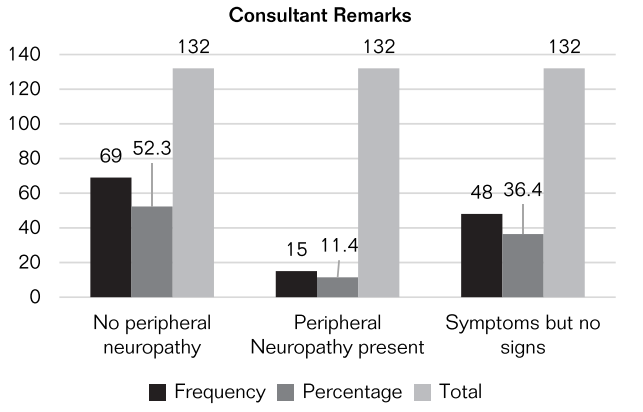
Information like name, age, gender, weight, height, was recorded. Patients were asked questions about osmolar symptoms, neuropathy symptoms like burning sensations, numbness and pricking etc. in peripheral organs especially feet, comorbidities and chronic use of medications causing neuropathy. Signs of neuropathy were diagnosed in these patients by Endocrinologist through standard clinical neurological examination using 128Hz tuning fork (vibration perception), tendon reflex testing and 10gm monofilament (touch sensation). IBM SPSS (version 27) was used for data analysis.

RESULTS

Clinical assessment showed three different groups among the 132 pre-diabetic patients: (Confirmed Neuropathy, Symptoms Only, and no Neuropathy). About 15 patients (11.4%) showed both symptoms and clinical signs of neuropathy (confirmed neuropathy), while 48 patients (36.4%) showed only neuropathic symptoms (mostly burning sensations) without clinical signs, suggesting early or subclinical neuropathy. Rest of the 69 patients (52.3%) showed no symptoms or signs of neuropathy.

FIGURE-1

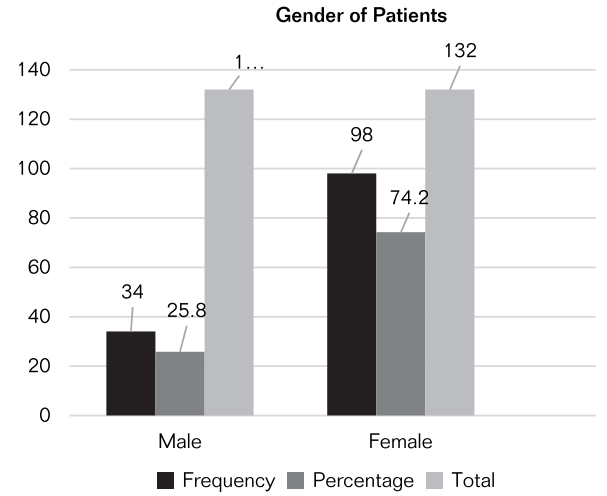
Prevalence of peripheral neuropathy



Among 132 pre-diabetic patients female participants predominated (n=98, 74.24%) compared to males (n=34, 25.76%).

FIGURE-2

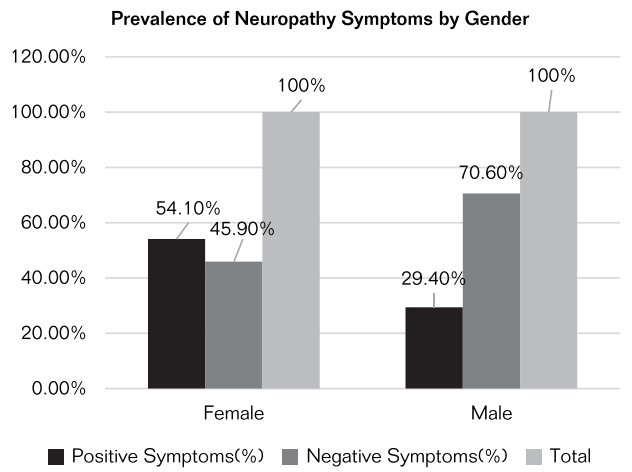
Gender distribution of study population



Our study found a strong link between gender and neuropathic symptoms. Female patients showed much more symptoms than males (54.1% vs 29.4%). This difference was statistically significant (X^2=6.158, p=0.013 and Fisher's p=0.017). These findings align with research studies about gender differences and nerve complications.

FIGURE-3

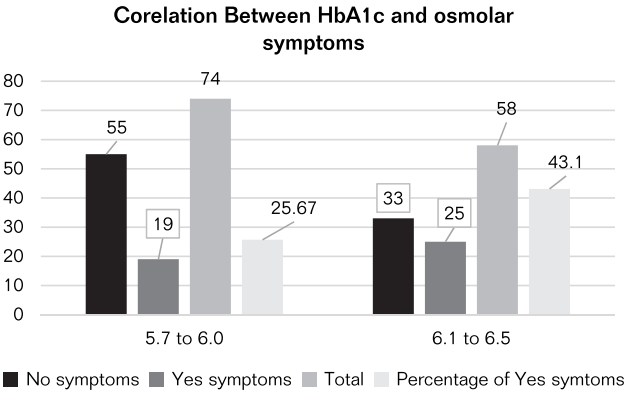
Prevalence of neuropathy symptoms by Gender:



Patients with higher HbA1c levels (6.1-6.5) showed significantly greater prevalence of osmolar symptoms (43.1%, n=25 out of 58) compared to those with lower levels (5.7-6.0) shows 25.7%, n=19 out of 74). This difference was statistically significant (X^2=4.444, p=0.035; Fisher's exact p=0.042). This correlation suggests that even within the pre-diabetic range, elevated HbA1c contribute to osmolar symptoms development.

FIGURE-4

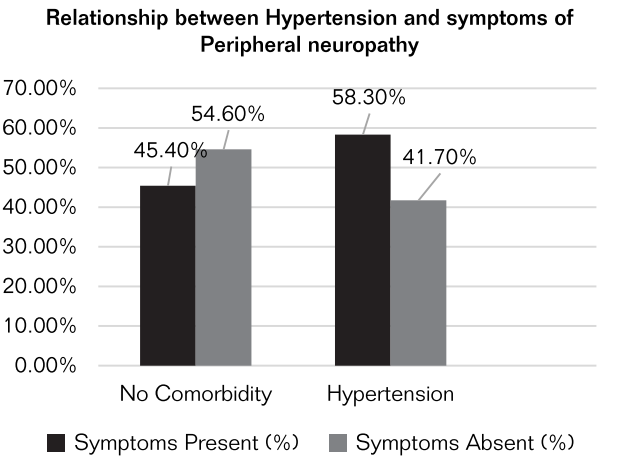
HbA1c and Osmolar symptoms association



Chi-square analysis showed no significant association between hypertension and neuropathic symptoms (X^2=1.323, p=0.250). While 58.3% of hypertensive patients reported symptoms compared to 45.4% of non-hypertensive patients (Fisher's exact p=0.268).

FIGURE-5

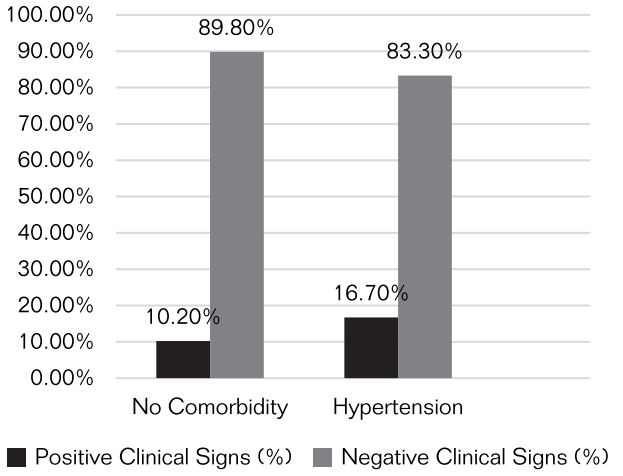
Hypertension and peripheral neuropathy correlations:



Chi square analysis revealed no significant association between hypertension and peripheral neuropathy (X^2=0.819, p=0.365), with 16.7% of hypertensive patients showing clinical signs while 10.2% of non-hypertensive patients (Fisher's exact p=0.474).

FIGURE-6

Relationship between hypertension and clinical signs of peripheral neuropathy



These trends align with some studies suggesting hypertension may increase microvascular complications, though our sample size was insufficient to detect such effects (Hypertension group: n=24).

DISCUSSION

Prediabetes is an intermediate hyperglycemic condition, where blood sugar levels are higher than normal but not high enough to be diagnosed as diabetes. As precursor to type 2 diabetes, its rising prevalence, much like diabetes itself, presents a significant challenge in managing disease burden and preventing complications.[9] Our study identified confirmed peripheral neuropathy in 11.4% of pre diabetic patients, with an additional 36.4% reporting neuropathic symptoms without clinical signs. These results are in accordance with a systematic review suggesting a wide range (2-77%) in terms of prevalence of peripheral neuropathy in prediabetic patients.[10] When assessed in detail for various regions of the world, it was found that the prevalence stood around 2% in United States (95% CI: 0%–4%).[11] but opposed to our study, only female population was assessed. In contrast, Brazil showed a high prevalence (77%) of peripheral neuropathy in prediabetic population (95% CI: 54%–100%).[12] This gross difference in terms of prevalence may be attributed to different methods used for detection of neuropathy in different studies.[13] The review article noted that majority of studies (21/29, 72%) reported prevalence of ≥10%[14], consistent with our confirmed cases (11.4%).

Our findings correlate with Papanas et al. 2011, who reported that 11-25% of pre diabetic individuals develop peripheral neuropathy.[15] According to a study conducted in India, the prevalence of peripheral neuropathy in prediabetic patients was observed around 30%.[16] It is important to note that apart from confirmed neuropathy cases detected on the basis of history and examination, our study also showed a significant number (36.4%) of patients who had symptoms of neuropathy but no clinical signs. This may suggest either early nerve damage or subclinical neuropathy. Our study showed female gender predominance (74% vs. 26%). also, Female prediabetic patients were found more prone to peripheral neuropathy as compared to male patients ((54.1% vs. 29.4%). This difference was statistically significant (X^2=6.158, p=0.013 and Fisher's p=0.017). These results are in accordance with a study conducted in Turkey where female prediabetic patients had an increased tendency to develop peripheral neuropathy.[17] This gross gender difference may be attributed to various hormonal changes or pain threshold difference in both genders.[18]

However, further studies to reveal this gross gender difference are needed. Our study also explored a significant association between HbA1c and osmolar symptoms. Patients with higher HbA1c levels (6.1-6.5%) showed high prevalence of osmolar symptoms (43.1%) compared to 25.7% in the lower HbA1c group (5.7- 6.0%, *p*=0.035). These results align with a study conducted in UK by Bulpitt et al. which revealed significant association between osmolar symptoms and glycemic markers (HbA1c & FPG) in diabetic patients. Dry mouth was strongly correlated with fasting plasma glucose (FPG) (p< 0.001) and marginally with HbA1c (p=0.05)[19]. Another study by Van der Does et al. (1996) shows that HbA1c > 6.1% linearly increases overall symptom burden including osmolar symptoms (RR: 1.02-1.36 times per 1% rise in HbA1c).[20] This similarity shows that even modest hyperglycemia within the prediabetic range can trigger osmolar symptoms, likely due to renal glucose spillage: According to

DeFronzo et al., 2015 higher HbA1c may exceed the renal threshold for glucose reabsorption, inducing osmotic diuresis.[21] Although Hypertensive prediabetic patients in our study exhibited slightly more neuropathy symptoms and signs, however this association was not statistically significant and further studies are needed in this regard. Our study has several limitations that should be considered for understanding its findings. First is the use of non-probability sampling technique, specifically a convenience sample of patients attending a single clinic that may introduce selection bias and limit the implications of these results to a wider population. Second limitation is the sample size, our sample size was relatively small (n=132), with a significant gender imbalance where female patients (n=98, 74.24%) were significantly more than male patients (n=34, 25.76%). Also our diagnostic techniques for screening of neuropathy were tuning fork for vibration sense, a tendon hammer for ankle reflexes, and a 10gm monofilament for touch sensation which are not as sensitive as standard tools like nerve conduction studies (NCS) or quantitative sensory testing (QST). Future research should aim to address these limitations by selecting more representative sampling methods and using standard diagnostic techniques for screening neuropathy.

CONCLUSION

As in diabetics, prediabetic patients can also develop peripheral neuropathy. Therefore, assessment of these patients for symptoms and signs of peripheral neuropathy must be conducted on initial visit.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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1	**Wajid Ullah Khan:** Study design.
2	**Tahir Ullah Khan:** Clinical supervision.
3	**Nafid Ullah Khan:** Manuscript review.
4	**Mohib Ullah Khan:** Data collection.
5	**Afaq Ahmed:** Data entry.
6	**Shefaat Ullah Shah:** Literature review.
7	**Waqas Ahmad Khan:** Data analysis.
8	**Shahfahad Ullah Khan:** Data interpretation.