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# Factors associated with diabetic peripheral neuropathy among adults with Diabetes Mellitus attending Kampala International University Teaching Hospital

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**ABSTRACT**

Diabetic Peripheral Neuropathy (DPN) is the most common type of Neuropathy and the commonest complication of Diabetes Mellitus contributing to major cause of non-traumatic foot amputation which has impact in substantial morbidity and mortality. Early detection of DPN with good glycemic control may prevent foot amputations. Epidemiological data about clinical presentation and factors associated with the development of DPN are not yet known in rural western Uganda. Therefore, the aim of this study is to determine the factors associated with DPN among adults with Diabetes Mellitus (DM) attending Kampala International University-Teaching Hospital (KIU-TH). A cross-sectional study which recruited 319 known DM patients was conducted in Internal Medicine Department and Diabetic Clinic at KIU-TH from December 2019 to March 2020 and from October to December 2020. Questionnaires were used to obtain clinical and sociodemographic data**,** neurological exam was done to assess the DPN and blood sample was collected from each participant for the determination of glycemic control (Glycosylated Hemoglobin). Data was analyzed using STATA version 15.0 while bivariate and multivariate logistic regression analyses were done to compare each independent variable with DPN (p-value*< 0.05).*The mean age of study participants was 59.4±13.6 years and females were 197(61.8%). Factors associated with DPN were DM duration of more than 10 years (aOR 4.6, 95% CI (2.36-8.9) p < 0.0001), use of both oral hypoglycemic agents and insulin (aOR 7.33, 95% CI (1.95-27.5), p = 0.003), and poor glycemic control (aOR 2.0, 95% CI (1.15-3.42), p = 0.013). Study participants who had DM duration of more than 10 years on both oral hypoglycemic agents and insulin with poor glycemic control were at an increased risk of developing DPN. Clinicians should start doing a peripheral neurological exam in all DM patients and awareness of heal.

**Keywords**: Factors, diabetes, peripheral and neuropathy.

## INTRODUCTION

The first recognition of Diabetes Mellitus was documented in the Egyptian ancient papyrus, discovered by Georg Ebers in 1862, dating back to 1550 BC which highlighted the first documented cases of DM over 3500 years ago as stated by Ebbell, in 1937 and Tattersall in 2010 [1]. The works of the 19th century (de Calvi, Pavy) established the link between diabetes mellitus and diabetic peripheral neuropathy [2]. Ancient texts describing what is believed to be diabetes mellitus represent clinical records of polyuric states in association with increased thirst, muscle wasting and premature death. In these early texts, neuropathic features of the clinical picture of diabetes can be found extremely rarely [1]. The epochal discovery of insulin in 1921 triggered a wide interest and more systematic approach to research of diabetic complications, leading to S. Fagerberger's conclusion that many of them share the underlying micro vascular pathology. It was not until the 18$^{th}$century that diabetic neuropathy was recognized as a common complication of diabetes and the subject of scientific interest and systematic studies [3]. The discovery of insulin had opened a new chapter in the history of diabetes and peripheral neuropathy. In the 1960s, Scientists used urine strip for

sugar level and the automated 'do it-yourself' measurement of blood glucose through glucometers, produced by Ames Diagnostics in 1969, brought glucose control from the emergency room to the patient's living room [2]. Routine blood sugar tests at prescribed intervals continued for a long time until the introduction of the glycosylated haemoglobin (HbA1c) estimation. That test, which measured blood glucose control over the previous three months (linked to the life of red blood cells), defined an extremely important aspect of diabetes management—tight control of blood glucose levels. The latter directly determined the risk of the occurrence of devastating complications of target organs like the eyes, vessels, nerves and kidneys that ultimately influenced morbidity and mortality [3]. It was not until the 1950s that the first oral antidiabetic drugs (sulphonylureas) were added to the treatment armamentarium [2]. Others, including metformin, glucosidase inhibitors and insulin sensitisers, followed in the succeeding decades with different sites of action to assure better handling and metabolic assimilation of ingested carbohydrates. In 1980, the first human insulin was discovered and manufactured by Graham Bell. The first biosynthetic insulin (humulin) was developed in 1982. Fifteen years later, there was introduction of the first needle-free insulin delivery system by Derata in 1979 provided relatively pain free, metered doses. Insulin pumps, inhaled insulin and oral sprays in recent times have shown the way ahead for easy administration [4]. [2], found that in the new millennium, pancreatic transplantation, first performed in 1966, exists as a radical treatment especially for intractable type one diabetes with advanced complications. Still in experimental mode, gene therapy with molecules like leptin and insulin may one day be a reality.

## Aim of study

To determine the Factors associated with diabetic peripheral neuropathy among adults with Diabetes Mellitus attending Kampala International University Teaching Hospital.

## Factors associated with diabetic peripheral neuropathy

Several factors have been associated with diabetic peripheral neuropathy and among them; socio-demographic and medical events with an impact in the occurrence and the development of DPN. [5] in their study done in Morocco found that female gender were associated with DPN. According to a sociological study done by [6] to assess a socio-ecological model in predicting diabetes self-care in America and Africa among diabetic patients demonstrated that diabetes is more common among women than men, and the number of women diagnosed with type 2 diabetes is increasing at a more rapid rate. Women seem to be especially vulnerable to diabetes complications. Engaging in diabetes self-care to reduce this risk of complications is also difficult for women. They experience higher expectation of fulfilling care-taking responsibilities, which may decrease time for self-care behaviors. Women have decreased equal employment and salary opportunities when compared to men, and they may not have as many financial resources to provide adequate diabetes self-care. It has been suggested that exposure to discrimination, higher rates of single female-headed households, increased poverty rate, and higher caretaker demands when compared to other ethnicities may influence African American women's vulnerability to disease [6]. [7] in a cross-sectional study which aimed to determine the risk factors and prevalence of DPN in Bangladesh among 294 diabetic patients revealed that the age more than 60 years was associated with peripheral neuropathy. Risk factors for diabetes complications include lack of physical activity, poor diet, overweight and obesity, poor care of feet, alcohol and tobacco use. These risk factors are highly modifiable through self-care regimens. Prescribed self-care behaviors include specific diet recommendations, exercise, smoking cessation, foot care, and monitoring/testing of blood glucose

levels [7]. A review done by [8] to assess DPN in India among T1DM and T2DM of 20 years and above showed that smoking, level of alcohol consumption were also associated with DPN among these diabetic patients. Factors such as cigarette smoking, alcohol, genetic predisposition, physical activity, life style change, poor hygiene, improper foot wear affected neuropathy in 331 diabetic patients of 30 years and above who attended the clinic and led to vascular disorders as well [9]. The most important risk factor for the development of diabetic peripheral neuropathy is hyperglycaemia [10]. [11] in their study found gender (more males than females), BMI ≥30Kg/$m^2$, duration of diabetes (more than 10 years) and poor glycemic control were associated with DPN. [7] in Bangladesh found that in 294 populations with DM, higher HbA1c, and longer duration of DM, retinopathy, hyperlipidemia, microalbuminuria and Hypertension were associated with DPN. They found also that some medications have been associated with DPN, especially when used in a long period in the treatment of DM, in association or separately. Long use of Insulin will induce neuritis (insulin-Neuritis/acute sensory neuropath) and metformin use among T2DM will induce peripheral neuropathy due to macrocytic anemia /vitamin B12 deficiency. [8] found out factors associated with DPN were obesity and diabetes duration of superior or equal to 10 years since the diagnosis. [12] conducted a cross-sectional study to assess the prevalence of DPN among adults with DM attending private and institutional outpatient clinics in South-Africa found that other factors linked to DPN include the patient's height, level of alcohol consumption and high cholesterol and triglyceride levels and type of Diabetes Mellitus. [13] in Cameroon found that determinants of DPN among DM patients were infection with hepatitis C virus, infection with HIV and presence of albuminuria. [14] carried out a cross-sectional study to describe the prevalence, the severity and factors associated with DPN in Uganda among adults' newly diagnosed diabetic patients demonstrated that the duration of diabetes, age of the subject, high blood pressure and history of smoking were important risk factors besides hyperglycemia in patients with Diabetic Peripheral Neuropathy.

## METHODOLOGY

### Study site

The study was conducted at Kampala International University Teaching Hospital (KIU-TH) in the Department of Internal Medicine. The department has 5 specialists, 17 senior house officers, 2 medical officers, 5 interns and 10 nurses. The medical out-patient department has a general, medical and private clinic conducted on a daily basis; diabetic and hypertension clinic conducted once a week mainly on Wednesday. That specialized clinic is led by a family medicine specialist who reviews all the Diabetic and Hypertensive patients.

### Study area

The study was conducted at KIU-TH. Kampala International University Teaching Hospital is located in Ishaka-Bushenyi municipality, western Uganda, a private non-profit hospital approximately 5 km away from Bushenyi district headquarters as well as Bushenyi Health Centre IV which is a government unit. The hospital is located in Ishaka town. Ishaka is a municipality in Bushenyi district and is found in Igara County, Bushenyi District, approximately 62 kilometers (39 miles) West of Mbarara district in western Uganda. The Internal Medicine department serves clients from the areas of Bushenyi, Sheema, Rubirizi, Mitooma and other neighboring districts in western Uganda.

### Population

The study population included all patients who attended the Medical outpatient clinic, diabetic clinic, general and private Outpatients department at KIU-TH.

### Target population

All known Diabetic patients in the catchment area of KIU Teaching Hospital.

### Accessible population

All patients with DM who presented to medical outpatient department, Diabetic

clinic, general and private outpatients department (KIU-TH) during the period of the study and who were aged 18 years and above.

**Study population**

All DM patients who presented in Internal Medicine department, Diabetic clinic, general and private outpatients department (KIU-TH) during the period of the study who were aged 18 years and above and accept to consent for the study.

**Sample size determination**

Sample size was calculated using [15].

$$N = \frac{Z^2 \, p \times q.}{d^2}$$

**N**=desired sample size for population greater 10,000.

**Z** $^2$=standard normal deviation, assuming a 95% confidence interval Z= 1.96.

**p**=proportion in the population estimated to have DPN in Uganda (Mulago Hospital, Kampala) =29.4% [14]

**q**= (1-p) = (1-0.294) =0.706.

**d**=Degree of accuracy for 95% confidence interval (0.05).

$$N = \frac{(1.96)^2 \times 0.294 \times 0.706}{(0.05)^2}$$

$$N = \frac{0.7973778624}{0.0025}$$

***N***=319 patients.

Internal medicine department receives about 18 diabetic patients per week (Medical outpatient department, DM clinic, General outpatient department, Private outpatient department combined) and approximately 70 patients per month.

**Sampling techniques**

Participants were consecutively enrolled until the target number was attained. Study participants were selected as they come to the outpatient clinics and DM Clinic. Details for the protocol which was used are shown in the flow chart (figure 1) below:

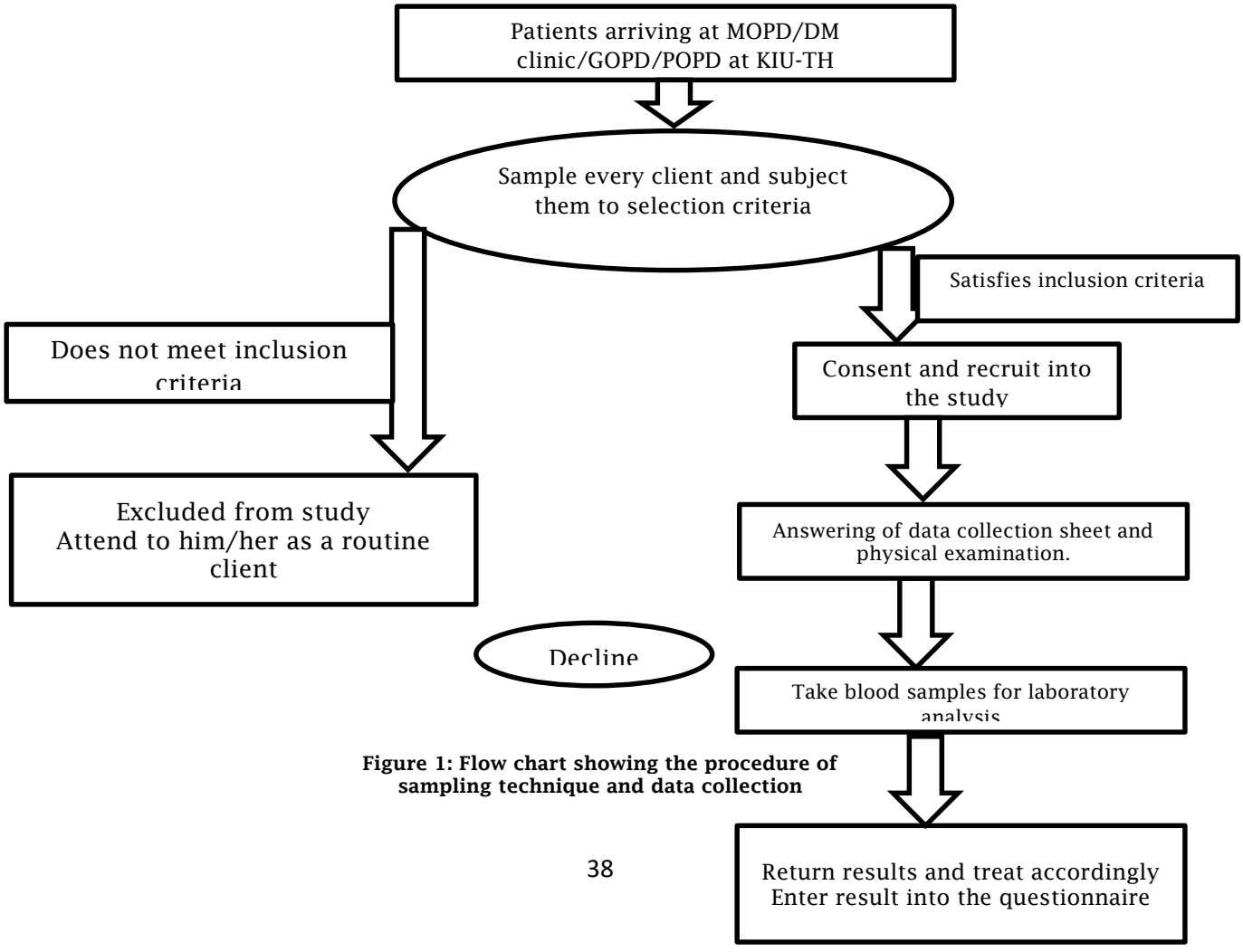


**Figure 1: Flow chart showing the procedure of sampling technique and data collection**

## Eligibility criteria

### Inclusion criteria

All adults (18 years and above) with DM who attended Internal Medicine department, DM clinic, General outpatient department and Private outpatient department during the duration of the study, and who provided a written consent to participate.

### Exclusion criteria

A patient was excluded from participation in the study if he/she had any mental disorders or was unable to withstand an interview or he/she changed his/her consent during the study. We excluded also all pregnant women, newly diagnosed DM patients at the time of interview and very sick DM patients admitted in Medical ward.

### Data collection method, tools and procedures

Data was collected using paper-based investigator-administered questionnaire that was designed in simple English and translated in Runyankole, based on the objectives and the conceptual framework. Patients were given information about the study, and then a written consent sought and signed. Demographics (age, sex, address, marital status, education status), history of chronic illness like hypertension, kidney disease, HIV, tuberculosis, social habits like use of alcohol and amount, smoking cigarette and number of sticks per day were taken, adherence to medication. We also asked about family history of DM, type of DM (from the history) and its duration, awareness of DM complications and DPN with its clinical presentation, practice of physical exercise and diet. Physical assessment of study participants included taking anthropometric measurements. These included: weight, height and Body Mass Index (BMI). The subjects' weight in kilograms was taken using a weighing scale manufactured by SECA®. Before the weight was taken, the subject took off his/her shoes and any heavy clothing. The weighing scale was calibrated every morning according to the manufacturer's manual, for those who cannot stand; a chair weighing scale was used. The height was recorded to the nearest 0.1 centimeter. The subject's height was measured using a SECA® wall mount station meter and a tape measure for those who could not stand. The height was recorded as the maximum distance from the floor to the highest point on the head. The BMI was calculated from a ratio of the patients' weight in kilogram to the square value of the height in meters. Normal BMI was defined as a value in between 18.5 and 24.9, overweight from 25 to 29.9, obesity from 30 and above [16]. Blood pressure was taken by using manual Sphygmomanometer with appropriate cuff sizes for the patient arms. High blood pressure was defined as systolic blood pressure ≥ l40 mmHg or diastolic pressure ≥ 90 mmHg. Using a sterile disposable syringe and needle, four (4) milliliters (mls) of blood was withdrawn from the anterior cubital fossa of each subject after cleaning with a swab soaked in 70% alcohol. Four (4) milliliters was placed in an EDTA (Ethylen diamine acetic acid) purple container for testing random/fasting blood sugar and glycosylated hemoglobin (HbA1c).

Furthermore, RBS/FBS was screened using a Control D glucometer machine made in India (2018) by Haiden technology with their respective glucose sticks. HbA1c was screened by using an Ichroma II Machine (2017) and the appropriated reagents for HbA1c. Each study participant received a printed copy of their RBS/FBS, HbA1c. The physical/neurological examination was done. Pressure sensation was assessed using 10g monofilament (Semmes westein test) at 4 of the 10 standard sites of the sole of the feet (plantar base of the big toe, 2nd and 5th toes and at the heel), avoiding areas with callosity. Vibration sense was elicited using a 128 Hz turning fork at the hallux of the big toe and Achilles deep tendon reflex was tested by using standard patellar hammer, both tools made in 2015(China). The Neuropathy Disability Score (NDS) and Diabetic Neuropathy Symptom Score

(DNS) were used in assessing the grade/degree of DPN for each patient. The NDS system is made of neuropathy score range from 0 – 10 which could also be used to assess severity of peripheral neuropathy by considering four(4) parameters: vibration sense by using a 128 Hz tuning fork(0=present,1=reduced/absent for each foot),temperature sensation by using a cold tuning fork(0=present,1=reduced/absent for each foot),pin-prick sensation by a monofilament test(0=present,1=reduced/absent for each foot and Ankle reflex/Achilles Tendon reflex by using a patellar hammer(0=normal,1=present with reinforcement,2=absent per side). Absence of Neuropathy (normal) was considered when the score was from 0 up to 2. The severity of neuropathy disability was graded as follows: mild (scores: 3–5), moderate (scores: 6–8), and severe (scores: 9–10). The NDS was validated and found to be 65% sensitive and 91% specific for diagnosing diabetic neuropathy [17]. For Diabetic Neuropathy Symptom Score (DNS), it is a four-item tool validated symptom score, with high predictive value to screen for Peripheral Neuropathy in diabetes. Symptoms of unsteadiness in walking, neuropathic pain, paraesthesia, and numbness are elicited. The presence of one symptom is scored as 1 point; the maximum score is 4 points. A score of 1 or higher is defined as positive for Diabetic Peripheral Neuropathy.

### Data collection instruments

We had a semi-structured questionnaire as a guide to conduct individual interviews. We used 10g monofilament test, patellar hammer, 128-Hz tuning fork/Hartman C 128 for the assessment of DPN as described above.

### Validity of data collection instrument

We used the Content Validity Index. This involved having five participants who were not part of the sample population and give them the questionnaire. The inter-participant agreement was then measured. The agreement of more than 70% was measured that the items of the questionnaire gave us the required information about DPN among DM patients.

### Reliability of data collection instrument

By using the Cronbach's coefficient alpha, a value of more than 0.8 was taken to indicate that items of the questionnaire were reproducible and consistent.

### Data quality control

Questionnaires were printed and pretested at KIU Teaching Hospital to ensure reliability and validity**.** We ensured that questionnaires were filled correctly by allowing enough time for response and filling. We also explained unfamiliar technical terms to the participants consistently. Questionnaires were also translated to the local language for easy understanding. For data completeness, the questionnaires were checked just after filling before they were taken for data entry and analysis. The blood samples were analyzed under KIU biochemistry laboratory in the hospital. It is well equipped to carry out the chemistry tests like FBS, HbA1c (Appendix VIII). Internal quality control was done for all samples and two samples were selected randomly and sent to a different certified laboratory in Uganda for external quality control (Lancet Laboratory/Mbarara).

### Data analysis plan and presentation

Data were captured in paper forms and entered into EPI INFO 7.2, Microsoft Excel version 2010 and exported into STATA 15.0 for analysis. Data were analyzed according to the specific objectives. It was processed accordingly and summarized using means for continuous variables or proportions for categorical variable.

### Ethical considerations

### Informed consent and respect for participants

Voluntary recruitment was done and an informed consent was signed. Informed consent from participants was obtained after fully explaining the details of the study to them in English and Runyakole (appendix III). Participants were not forced to enroll themselves and were free

to withdraw from the study at any time they wished without coercion or compromising of care that they were entitled to.

**Risks and adverse events to study participants**

Study participants underwent mild pain during pricking. There was also a potential risk to introduce infection during the process of draining blood from participants. However, the process of obtaining a blood sample was done gently and professionally by a phlebotomist to minimize risk of pain and minimize infection as far as possible. Additionally, 10g monofilament test, tuning fork and patellar hammer were used for neurological assessment according to standard local and international guidelines. No complications were expected during the study, there was no need for reimbursement for any damages.

**Benefits of the research**

The benefits of doing a full peripheral neurological exam and measuring the HbA1c among DM patients led to early diagnosis and medical treatment, which reversed foot amputation as outcome of DPN. The community benefited from laboratory tests at no cost of the patient.

**Privacy and confidentiality**

Identification of participants was by means of numerical codes. Details of respondents were kept under lock and key for privacy and confidentiality purposes throughout the course of research. Respect of the respondents' rights and fair treatment were strictly adhered to, thus minimizing harm and discomfort to them. There was no disclosure of participants' information to the public without their consent and all identities were removed from the results.

**Selection of participants**

All participants were given equal opportunity to participate in the study. Priority was not given in terms of tribe, interest group, race or religion. Systematic random sampling method was used to select participants and ensure equal chance of being selected for the study. Eligibility criteria were strictly adhered to.

**Incentives and reimbursement**

No monetary or any other form of incentives was offered to the participants but compensation and reimbursement was offered where applicable.

**Approval procedure**

Approval to carry out the study was sought from the department of Internal Medicine, the Faculty of Clinical Medicine and Dentistry and Directorate of post-graduate studies and finally the Research Ethics Committee of Kampala International University. All ethical documents were presented to the administration of Kampala International University Teaching Hospital before the study to be conducted and administrative clearance was obtained before commencement of the study.

**Respect for community**

The procedures involved in this study were not against the local community beliefs, traditions and culture. The findings from the study were communicated to the head of internal medicine department of Kampala International University Teaching Hospital as a formal feedback as well as office of District Health Officer, Bushenyi district so that the community can benefit from it.

**Limitations**

Poor cooperation or withdrawal of consent from some participants during the study.

**Solution**: Comprehensive counselling of participants with regards to the participation.

Lack of some other specific but unavailable investigations, such us electrophysiological tests, for assessing diabetic peripheral neuropathy.

**Solution:** Use of monofilament test, other tools and standard scores for neuropathy in order to overcome that limitation.

## RESULTS

**Study participants profile**

Overall, 338 participants arrived at MOPD, DM clinic, GOPD and POPD at KIU-TH, 5 participants were excluded from the study because 3 were newly diagnosed DM and 2 were very sick. The participants who met the inclusion criteria were 333 and among them, 5 declined to consent

and 9 declined the examination and the blood sample collection, finally 319 study participants consented and filled the study questionnaire, were examined and their blood sample taken during the study period and analyzed.

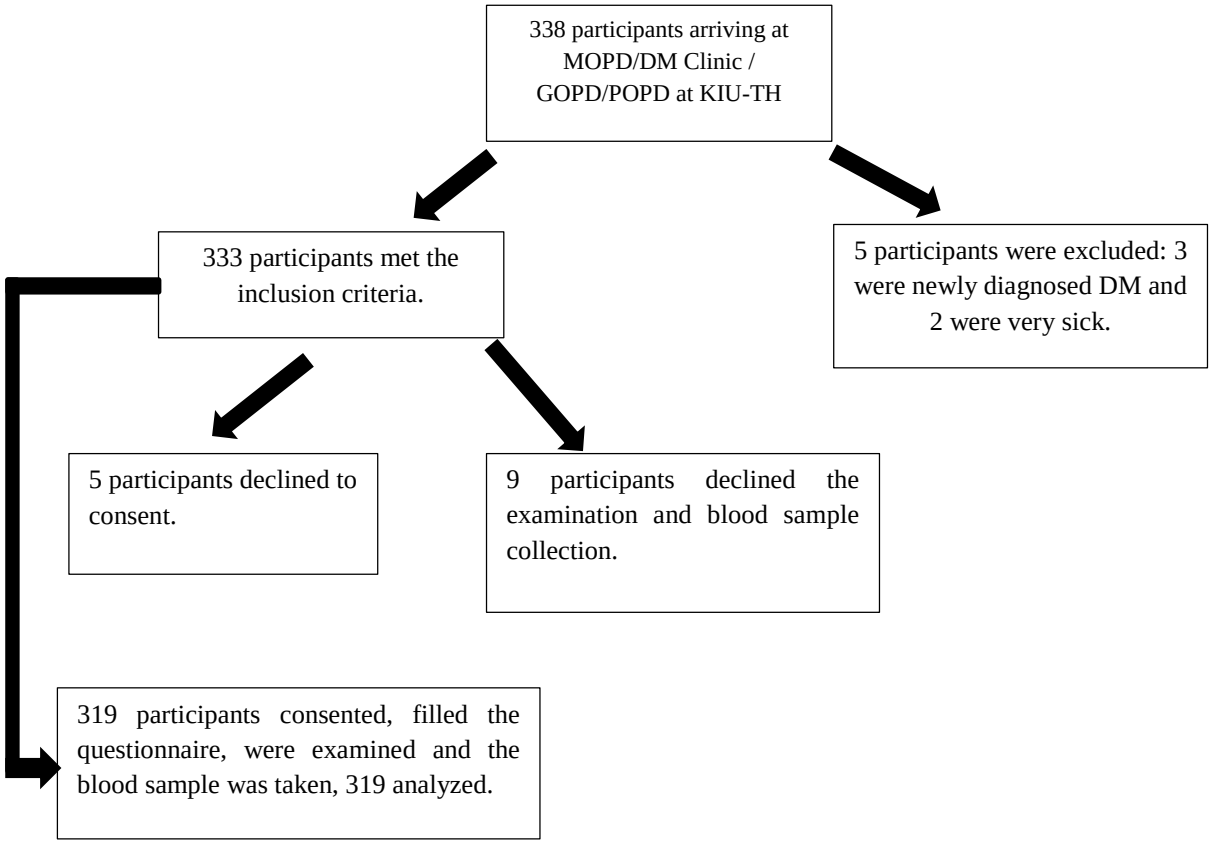


**Figure 2. Study participants profile**

**Baseline characteristics of study participants of adults with Diabetes Mellitus attending Kampala International University Teaching Hospital.**

**Table 1. Baseline characteristics of the study participants**

| Baseline Characteristics | N=319 |
|---|---|
| Sociodemographic characteristics | |
| Age, mean (±SD) | 59.4 (±14.6) |
| Female, n (%) | 197 (61.8) |
| Rural residence, n (%) | 272 (85.3) |
| Married, n (%) | 267 (83.7) |
| Education level, n (%) | |
| Primary | 129 (40.4) |
| Secondary | 35 (10) |
| None | 137 (42.9) |
| Occupation, n (%) | |
| Peasants | 248 (77.7) |
| Private business | 22 (6.9) |

| | |
|---|---|
| Professional | 22 (6.9) |
| Behavioral factors, n (%) | |
| Alcohol (Audit Score), n (%) | |
| Audit 1 | 35 (10) |
| Audit 2 | 31 (9.7) |
| Smoking | 43 (13.5) |
| Medical factors, n (%) | |
| DM duration, mean (±SD) | 7.33 (±6.40) |
| < 10 years | 209 (65.5) |
| ≥ 10 years | 110 (34.5) |
| Types of Diabetes Mellitus, n (%) | |
| Type 1 DM | 15 (4.7) |
| Type 2 DM | 304 (95.3) |
| Diabetic therapy, n (%) | |
| Oral hypoglycemic agents | 203 (63.6) |
| Insulin | 41 (12.9) |
| Both Oral hypoglycemic agents + insulin | 57 (17.9) |
| Not on diabetic therapy | 3 (5.6) |
| BMI, mean (±SD) | 26.26 (±3.48) |
| BMI Categories (Kg/m$^2$), n (%) | |
| Normal (18.5 - 24.9) | 103 (32.3) |
| Overweight (25.0 - 29.9) | 178 (55.8) |
| Obese (≥30) | 38 (11.9) |
| HbA1c percent, mean (±SD) | 7.61 (±2.47) |
| HbA1c percent, n (%) | |
| Good glycemic control (<7.0) | 147 (46.1) |
| Poor glycemic control (≥ 7.0) | 172 (53.9) |
| Fasting glucose (mmol/l), mean (±SD) | 10.35 (±5.16) |
| Systolic BP (mmHg), mean (±SD) | 138.4 (±19.77) |
| Diastolic BP (mmHg), mean (±SD) | 85.8 (±12.95) |
| Hypertension, n (%) | 160 (50.2) |
| HIV, n (%) | 29 (9.1) |

In table 1, majority of the study participants were females (61.8%) and most of them were married (83.7%), residing in rural area (85.3%) with mean age of 59.4 ± 14.6 years and were peasants by occupation (77.7%). Also, most of them were T2DM (95.3%) on oral hypoglycemic agents (63.6%), overweight (55.8%) with mean BMI of 26.26 ±3.48 and poor glycemic control (53.9%) with DM duration of less than 10 years (65.5%),mean duration of 7.33 ±6.40 years. A few study participants were taking alcohol/Audit Score 1 (10%) with history of smoking (13.5%) and hypertension (50.2%).

**Bivariate and Multivariate analysis of factors associated with Diabetic Peripheral Neuropathy among adults with Diabetic Mellitus attending Kampala International University Teaching Hospital**

**Table 2: Bivariate and multivariate logistic regression analysis**

| | Diabetic Peripheral neuropathy | | | |
|---|---|---|---|---|
| | Crude analysis | | Adjusted analysis | |
| **Variable** | **cOR (95% CI)** | **P value** | **aOR (95%CI)** | **p-value** |
| **Gender** | | | | |
| Female | 1.21 (0.75-1.94) | 0.4219 | 1.16 (0.66-2.05) | 0.121 |
| **Age( years)** | | **0.0392** | | |
| 18-49 | 1.0 | - | - | - |
| ≥50 | 1.8 (1.03-3.02) | - | 1.70 (0.86-3.34) | 0.076 |
| **Smoking** | 0.79 (0.41-1.53) | 0.5044 | 0.66 (0.30-1.43) | 0.295 |
| **Alcohol (Audit Score)** | | 0.8185 | | |
| **Audit 0** | 1.0 | - | - | - |
| **Audit 1** | 1.12 (0.52-2.40) | - | 1.23 (0.51-3.0) | 0.636 |
| **Audit 2** | 0.81 (0.37-1.75) | - | 0.61 (0.25-1.50) | 0.287 |
| **Duration of DM** | | | | |
| < 10 years | 1.0 | - | - | - |
| ≥ 10 years | 5.19 (2.85-9.46) | < **0.00001** | 4.6 (2.36-8.9) | < **0.0001** |
| **DM types** | | 0.1192 | | |
| Type 1 | 1.0 | - | - | - |
| Type 2 | 2.29 (0.81-6.51) | - | - | - |
| **Diabetic therapy** | | **0.0003** | | |
| Not on medications | 1.0 | - | - | - |
| Oral hypoglyc. Agents | 4.73 (1.62-13.80) | - | 2.94 (0.94-9.13) | 0.062 |
| Insulin | 5.01 (1.48-16.92) | - | 2.37 (0.61-9.2) | 0.211 |
| Both oral hypo. ag+Insulin | 12.22 (3.54-42.09) | - | 7.33 (1.95-27.5) | **0.003** |
| **BMI categories (Kg/m²)** | | 0.6625 | | |
| Normal (18.5-24.9) | 1.0 | - | - | - |
| Overweight (25.0-29.9) | 1.24 (0.74-2.06) | - | 1.11 (0.62-1.2) | 0.717 |
| Obese (≥30) | 1.0 (0.46-2.16) | - | 1.0 (0.41-2.45) | 0.983 |
| **Poor GlyC (HbA1c ≥ 7%)** | 2.05 (1.28-3.28) | **0.0025** | 2.0 (1.15-3.42) | **0.013** |
| **Hypertension** | 1.53 (0.96-2.44) | 0.0698 | 1.46 (0.84-2.56) | 0.165 |
| **HIV** | 0.98 (0.44-2.19) | 0.9702 | - | - |

***P value is significant at < 0.05, cOR= Crude odds ratio. aOR= adjusted odds ratio***

In table 2, in the bivariate analysis, study participants aged of 50 years and above were 1.8 time more likely to have Diabetic Peripheral Neuropathy compared to those

who were aged less than 50 years (cOR 1.8, 95 %, (CI=1.03-3.02), p = 0.039).

In the multivariate analysis, study participants who had DM duration of more than 10 years since the diagnosis were 4.6 times more likely to have DPN compared to those with the duration of DM since the diagnosis of equal or less than 10 years (aOR 4.6, 95%, (CI=2.36-8.9), p < 0.0001). Participants who were on both oral hypoglycemic agents and Insulin had 7.3 times risk of having DPN than those who were on oral hypoglycemic agents and Insulin alone and those who were not on any medication (aOR 7.33, 95%, (CI=1.95-27.5), p = 0.003). Participants with poor glycemic control (HbA1c ≥ 7%) were 2 times more likely to have DPN compared to those who had a good glycemic control (HbA1c < 7%) (aOR 2.0, 95%, (CI=1.15-3.42), p = 0.013).

## DISCUSSION

### Factors associated with diabetic peripheral neuropathy among adults with Diabetes Mellitus attending Kampala International University Teaching Hospital

In our study, age more than 50 years was associated with Diabetic Peripheral Neuropathy. The medical factors associated with Diabetic Peripheral Neuropathy are diverse and complex. In this study, duration of more than 10 years since the diagnosis of DM, poor glycemic control and use of both oral hypoglycemic agents and Insulin were independently associated with DPN. The findings above are not different from those studied by [11] in a meta-analysis done in US, UK, France, Belgium and South-Africa (2018) where advanced age were significantly associated with the occurrence of Peripheral Neuropathy. [7] in Bangladesh (2010) found also the same. Diabetic peripheral neuropathy develops progressively over months to years and by the time aging process is taking place; there is decrease in peripheral nerves function, mostly in lower extremities with physical disabilities, gait disturbance and falls. Our findings were also similar to those of [11] who carried out a meta-analysis in United Kingdom, United States of America, in Belgium, in France and in South Africa and from the MENA (Middle East and North Africa: Saudia Arabia, Turkey, Algeria, Egypt, Lebanon, Jordan, Gulf States) and the results showed DM duration of more than 10 years were also strongly associated with DPN. This was congruent with the findings from our study because the meta-analysis above considered a large sample in many regions, even in poor and developed countries where we have almost the same realities. Moreover, since the Diabetic Peripheral Neuropathy is a chronic complication, peripheral nerve damages are expected with the time as the disease is progressing.

The most important risk factor for the development of DPN is hyperglycemia [10]. In India [8], found that good glycemic control delays the progression of diabetic peripheral neuropathy in Diabetes Mellitus. This is similar to our study where poor glycemic control was also associated with Diabetic Peripheral Neuropathy, reasons being that hyperglycemia has been regarded as the a great culprit for the initiation of metabolic cascade and molecular derangements that result in degenerative phenomena plus a potential progressive neurological deficits. Our study has showed that diabetic therapy has also an impact in the occurrence of DPN: patients who are using both oral hypoglycemic drugs and insulin therapy are likely to have DPN compared to those on oral hypoglycemic agents and insulin separately and those not on any medication as well. This could be explained by the fact that most of our study participants were on oral medications for type 2 DM and Metformin was the first line drug commonly used, which can induce peripheral neuropathy by vitamin B 12 deficiency. Similar findings were published by [18] revealing that patients with type 2 DM may develop features of DPN as a consequence of Metformin induced vitamin B 12 deficiency and some of these patients were asymptomatic. In our study, combined long term use of insulin and

oral anti diabetic medications is responsible of insulin-Neuritis, a form of DPN that occurs in all types of Diabetes due to prolonged hyperglycemia with micro vascular complications. It refers to what is called "Treatment induced neuropathy in diabetes", as an iatrogenic diabetic peripheral neuropathy and therefore Metformin alone or in association with insulin is an associated factor of DPN [19].

## CONCLUSION

Study participants who had DM duration of more than 10 years since the diagnosis, on both oral hypoglycemic agents and insulin with poor glycemic control were at an increased risk of having DPN.

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