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Clinical presentation of 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 clinical presentation 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%). Pain and paresthesia were the most common clinical presentation of DPN (90%). The most common Clinical Presentation of DPN among DM patients attending KIU-TH were pain, paresthesia, numbness, muscle weakness, loss of balance and pain less foot ulcers. Clinicians should start doing a peripheral neurological exam in all DM patients and awareness of health personnel about factors associated with DPN.

Keywords: Clinical presentation, Diabetes and Peripheral

INTRODUCTION

The works of the 19th century (de Calvi, Pavy) established the link between diabetes mellitus and diabetic peripheral neuropathy [1]. 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 [2]. 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 18thcentury 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 [1]. 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].

Aim of the Study

To determine the Clinical presentation of Diabetic Peripheral Neuropathy among adults with Diabetes Mellitus attending Kampala International University Teaching Hospital

Clinical presentation of diabetic peripheral neuropathy

The diagnosis of DPN is made of many syndromes; the most common type is distal symmetric sensorimotor polyneuropathy [4]. The typical presentation of DPN is symmetrical "stocking and gloves" distribution and is often associated with nocturnal exacerbation [5]. They can be cutaneous hypersensitivity leading to acute distress on contact with any external stimulus (allodynia), defined as pain that is caused by a stimulus that does not normally cause pain [6]. [7] described, in a clinical communication that pain was the predominant features of DPN and that pain can be worse at night disturbing sleep, causing tiredness during the day, distressing allodynia, and severe pain in the legs has also been reported. Approximately 40% of patient visiting a primary care setting who have DPN complain about pain and 20 % of them have had pain for greater than 6 months [8]. Pain related to DPN is often difficult to manage and it is associated, most of the time with mood and sleep disturbances. The primary symptom of DPN is loss of sensation in the toes, which extends to involve the feet and leg in a stocking distribution. Some patients complain about numbness sensation and pain, but most frequently the disease progresses insidiously and undetected [9]. [9] in Bangladesh reported that the risk of diabetes related amputations and the prevalence of diabetic foot ulcers are significantly lower in Asians compared to Europeans. In addition, the foot ulcers among diabetic patients are mostly of neuropathic origin, and therefore eminently preventable. Up to 85% of amputations among diabetic patients are preceded by foot ulcer. [10] did a cross-sectional study to evaluate peripheral neuropathy in diabetic adults with and without foot ulcers in Nigeria that involved 90 diabetic adults, 45 with foot ulcers and 45 without foot ulcers obtained a value of 80% in DPN patients with foot ulcers and they showed that advancing age is an independent risk factor for the development of peripheral neuropathy which can lead to food ulcer. [11] did a cross-sectional study to evaluate DPN in Arabia among patients aged between 40-69 years demonstrated that DPN was present in 36.6% of the population, foot ulceration in 5.9% and peripheral vascular disease (PVD) in 11.8%. According to [9] in a clinic-based study, large proportions of the DM patients have neuropathic complications and were at potential risk of developing foot lesions. Patients with DPN are two to three times more likely to fall than diabetics without neuropathy. This is not a late-stage complication; the increased risk of falls has been noted 3 to 5 years prior to their diagnosis. Moreover, those with neuropathy have a 15% increased risk of developing ulcers during their disease course and 6 to 43% of those with ulcers will eventually have an amputation [9]. DPN is a leading cause for disability due to foot ulceration and amputation, gait disturbance, and fall-related injury [7]. Approximately 15% of DM patients develop at least one foot ulcer during their lifetime; although vascular disease has a role in the occurrence of diabetic foot ulcers, around 60%-70% of diabetic foot ulcers are primarily neuropathic in origin [12]. Studies conducted in the Middle East Region (MER) by [11] shown high rates of painful DPN, ranging from 35% to 65%. Patients with DPN account for more hospital admissions than all other DM complications combined, and are

responsible for 50%-75% of non-traumatic limb amputations [11]. About 20 to 30% of patients with DPN suffer from neuropathic pain [12]. Diabetic peripheral neuropathy is an important risk factor for diabetic foot ulceration and majority of diabetic patients with this peripheral nerve damage are asymptomatic; hence foot ulcer may be the first clinical presentation or a late complication of DPN if there is no adequate treatment [13]. Conceptually, the above studies described few clinical presentation of DPN or did not describe them at all. Some studies assessed only the severity of DPN [13]. Contextually, most of previous studies were conducted among newly diagnosed diabetic patients. These gaps were filled in our research by setting a brief systematization of clinical features of DPN and focusing on known diabetic patients.

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 [14].

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

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% [15]

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:

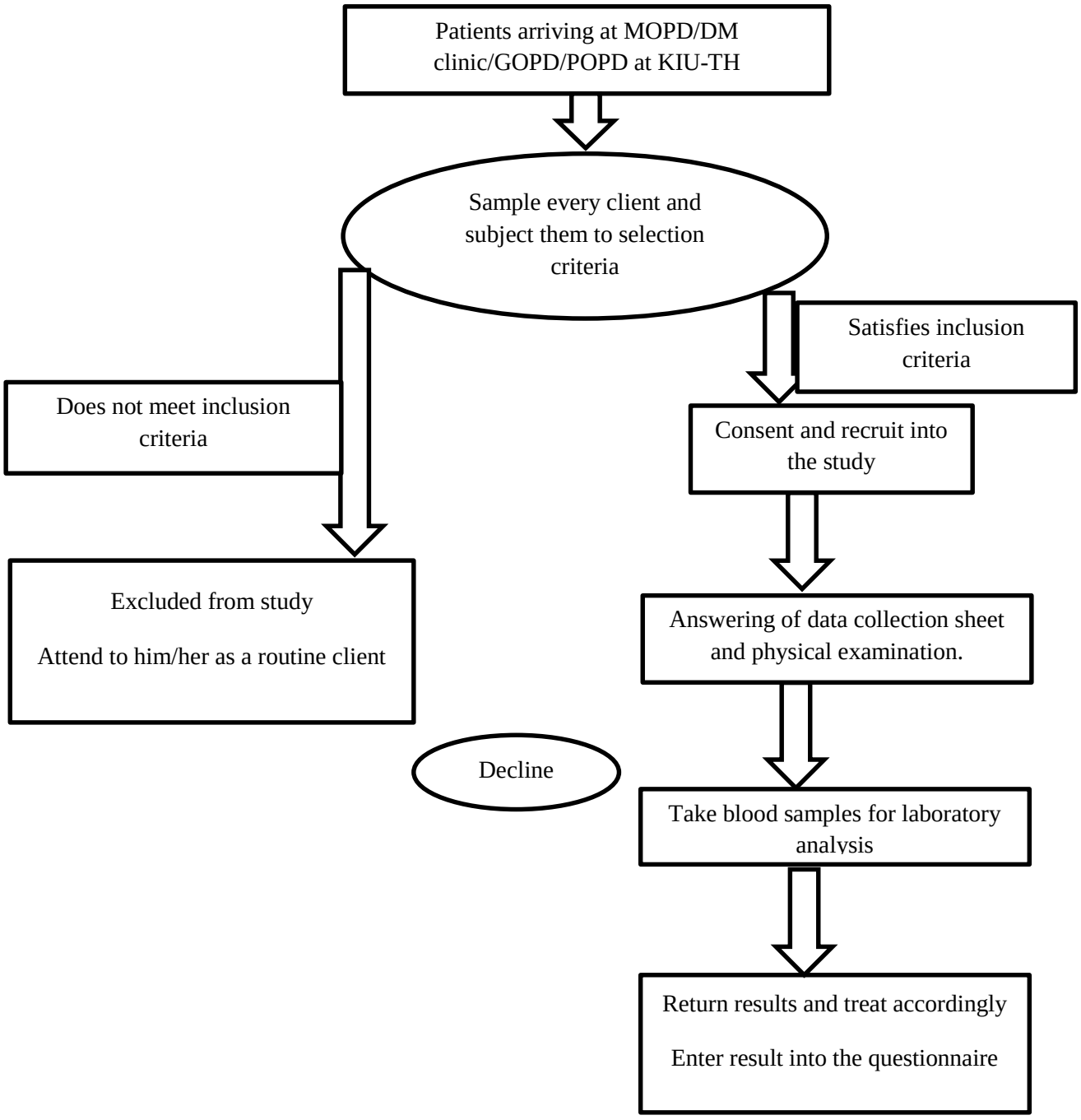

Figure 1: Flow chart showing the procedure of sampling technique and data collection

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 (WHO, 2000). 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 [16]. 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.

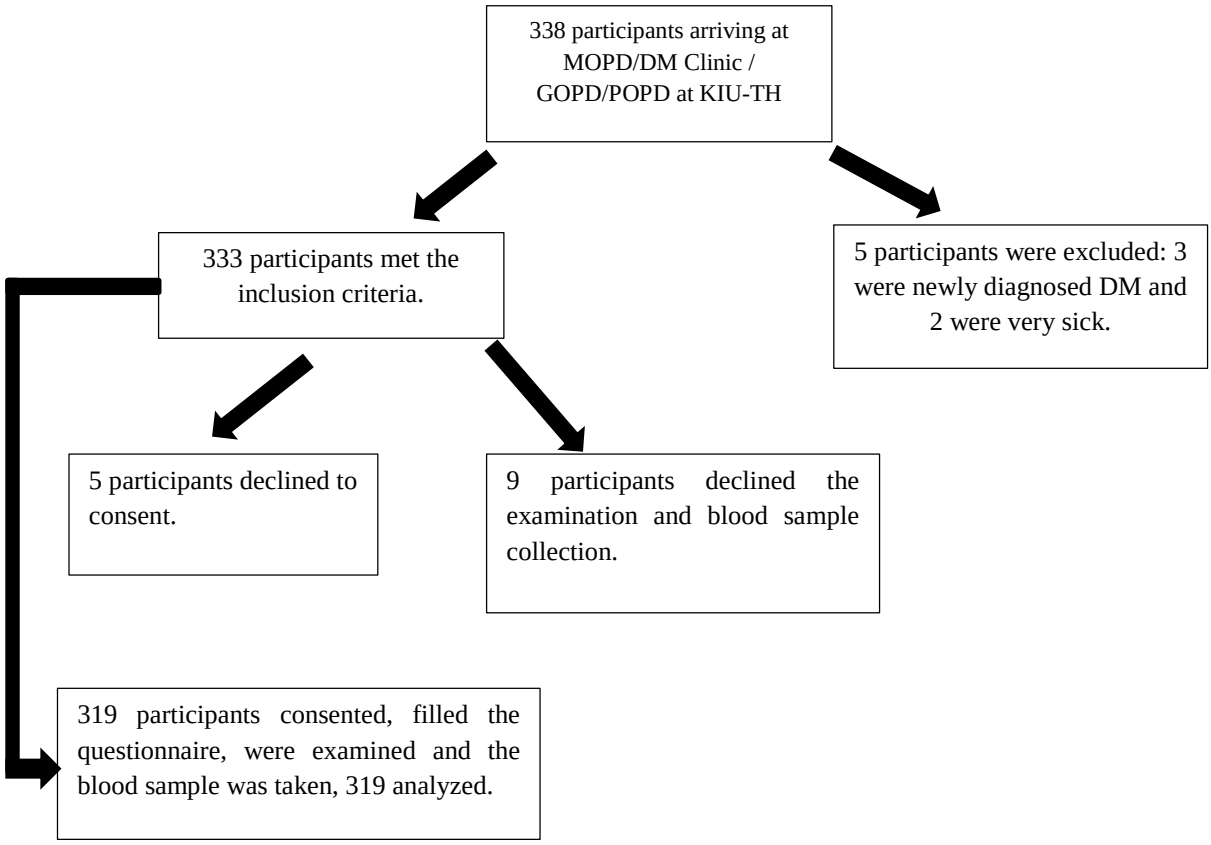

Figure 2. Study participants profile

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%).

Clinical presentation of diabetic peripheral neuropathy among adults with Diabetes Mellitus attending Kampala International University Teaching Hospital

Table 2. Clinical presentation of DPN among adults with DM attending KIU-TH

Clinical presentation of DPN	N=210
	n (%)
Symptoms	
Pain	189 (90)
Numbness	152 (72.4)
Paresthesia	189 (90)
Muscle weakness	75 (35.7)
Signs	
Loss of balance	61 (29)
Painless foot ulcers	23 (11)

In table 2, pain (90%) and paresthesia (90%) were the most common clinical presentation of DPN among adults with DM attending Kampala University-Teaching Hospital, followed by numbness (72.4%), muscle weakness (35.7%), loss of balance (29%) and pain less foot ulcers (11%).

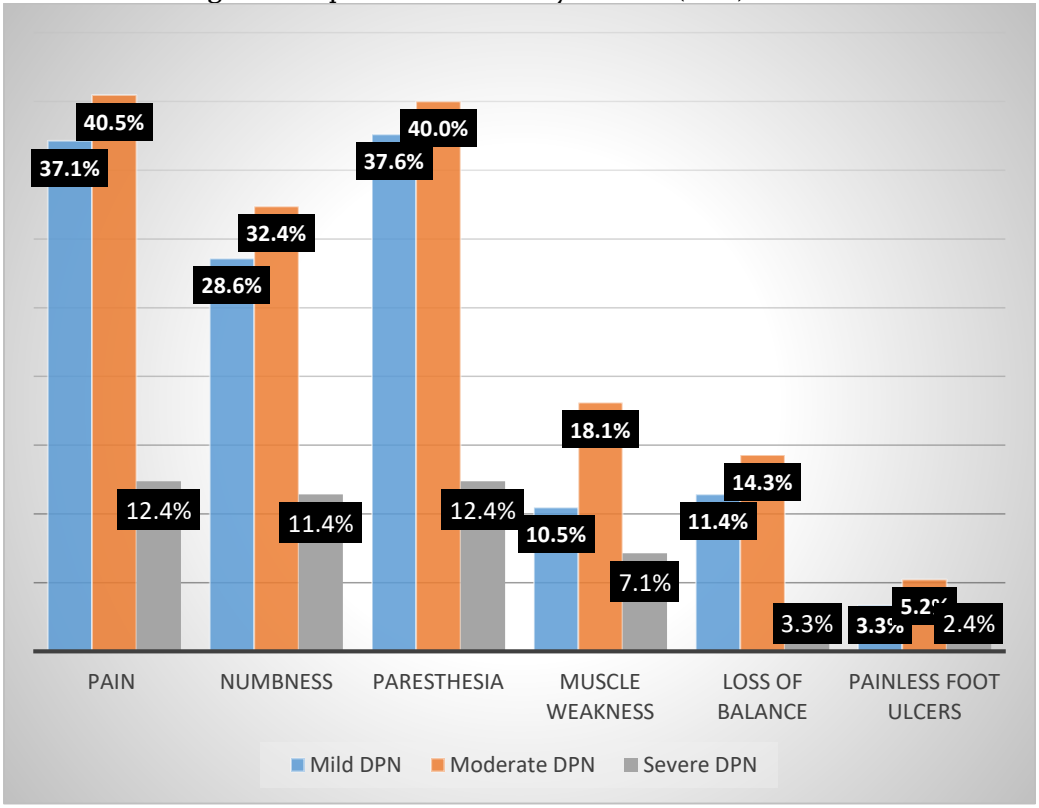

Figure 3. Clinical presentation of DPN and NDS

In figure 3, clinical presentation is presented based on the severity of DPN. Most of the Study participants who had pain and paresthesia developed respectively mild DPN (37.1%) and moderate DPN (40%). Few participants who had painless foot ulcers developed severe DPN (2.4 %).

DISCUSSION

Clinical presentation of Diabetic Peripheral Neuropathy among adults with Diabetes Mellitus attending Kampala International University Teaching Hospital

In our study, the most common clinical presentation was pain and paresthesia followed by numbness sensation, muscle weakness, loss of balance and pain less foot ulcers. In United Kingdom, [17] and [6] revealed the common features of DPN were also pain and paresthesia respectively. This could be because most of Diabetic patients complain of pain on the feet/lower limbs with different variants (allodynia, hyperesthesia, hyperalgesia, dysesthesia) and other characteristics. However, in a study done in Bangladesh by [9] and another one done by [11] in Arabia found that the most common clinical feature of Diabetic Peripheral Neuropathy among diabetic patients was foot ulcer. The discrepancy with this current study could be because the two studies above focused on the assessment of risk of amputation in patients with diabetic neuropathy. In a study done in Morocco [4], "stocking and gloves" pain distribution and loss of sensation were the most predominant clinical presentation. This is different from our study and that could be because this study used the Diabetic Neuropathy Symptom (DNS) Score and the Neuropathy Disability Score (NDS) with standardized varieties of subjective and objective clinical manifestation of Diabetic Peripheral Neuropathy. In Uganda (Kampala), majority of patients with Diabetic Peripheral Neuropathy were asymptomatic and few of them had foot ulceration as complaint [13]. This is different from the findings of our study because, the one done in Kampala was interested in the severity of Diabetic Peripheral Neuropathy without classifying its different clinical features.

CONCLUSION

The most common Clinical Presentation of DPN among DM patients attending KIU-TH was pain and paresthesia, followed by numbness, muscle, weakness, loss of balance and pain less foot ulcers.

REFERENCES

1. Zajac, J., Shrestha, A., Patel, P. and Poretsky, L. (2010).The main events in the history of diabetes mellitus. *Principles of diabetes mellitus* .Springer, Boston, MA, 3 - 16.
2. Nwaneri, C. (2015). Diabetes mellitus: A complete ancient and modern historical perspective. Webmedcentral, 28.
3. Skljarevski, V. (2007). Historical aspects of diabetic neuropathies.In *Diabetic Neuropathy* (pp. 1-5). Humana Press, 2.
4. Chahbi, Z., Lahmar, B., El Hadri, S., Abainou, L., Kaddouri, S., Qacif, H. and Zyani, M. (2018). The prevalence of painful diabetic neuropathy in 300 Moroccan diabetics.*The Pan African Medical Journal*, *31-158*.
5. Feldman, E. L. (2012). Pathogenesis and prevention of diabetic polyneuropathy.*UpToDate. Waltham*.
6. Garoushi, S., Johnson, M. I. and Tashani, O. A. (2018). Point prevalence of painful diabetic neuropathy in the Middle East and North Africa region: A systematic review with meta-analysis. *Libyan Journal of Medical Sciences*, *2*(3), 85.
7. Callaghan, B. C., Cheng, H. T., Stables, C. L., Smith, A. L. and Feldman, E. L. (2012). Diabetic neuropathy: clinical manifestations and current treatments. *The lancet, 11*(6), 521-534.
8. Vinik, A. I., Erbas, T. and Casellini, C. M. (2013).Diabetic cardiac autonomic neuropathy, inflammation and cardiovascular disease. *Journal of diabetes investigation*, *4*(1), 4-18.

9. Mørkrid, K., Ali, L. and Hussain, A. (2010). Risk factors and prevalence of diabetic peripheral neuropathy: a study of type 2 diabetic outpatients in Bangladesh. *International journal of diabetes in developing countries*, *30*(1), 11.
10. Ede, O., Eyichukwu, G. O., Madu, K. A., Ogbonnaya, I. S., Okoro, K. A., Basil-Nwachuku, C. and Nwokocha, K. A. (2018). Evaluation of Peripheral Neuropathy in Diabetic Adults with and without Foot Ulcers in an African Population.*Journal of Biosciences and Medicines*, *6*(12), 71-78
11. Noor, M. J. and Moiz, B. (2015). Diabetic Peripheral Neuropathy;A common complication in Diabetic patients. *Bahrain Medical Bulletin*, vol.37,1.
12. Jacovides, A., Bogoshi, M., Distiller, L. A., Mahgoub, E. Y., Omar, M. K., Tarek, I. A. and Wajsbrot, D. B. (2014). An epidemiological study to assess the prevalence of diabetic peripheral neuropathic pain among adults with diabetes attending private and institutional outpatient clinics in South Africa.*Journal of International Medical Research*, *42*(4), 1018-1028.
13. Kisozi, T., Mutebi, E., Kisekka, M., Lhatoo, S., Sajatovic, M., Kaddumukasa, M. and Katabira, E. (2017). Prevalence, severity and factors associated with peripheral neuropathy among newly diagnosed diabetic patients attending Mulago hospital: a cross-sectional study. *African health sciences*, *17*(2), 463-473.
14. Kish, Leslie (1965): Survey Sampling. New York: John Wiley and Sons, Inc. p. 78-94
15. Kisozi, T., Mutebi, E., Kisekka, M., Lhatoo, S., Sajatovic, M., Kaddumukasa, M. and Katabira, E. (2017). Prevalence, severity and factors associated with peripheral neuropathy among newly diagnosed diabetic patients attending Mulago hospital: a cross-sectional study. *African health sciences*, *17*(2), 463-473.
16. Dyck, P. J., Bushek, W., Spring, E. M., Karnes, J. L., Litchy, W. J. and O'Brien, P. C. (1987). Vibratory and cooling detection thresholds compared with other tests in diagnosing and staging diabetic neuropathy. *Diabetes care*, *10*(4), 432-440.
17. Vinik, A. I. (2016). Diabetic sensory and motor neuropathy. *New England Journal of Medicine*, *374*(15), 1455-1464.