Prevalence and Association of Microvascular Complications with some clinical Factors in Patients with Type 2 Diabetes Mellitus in Kano, Nigeria

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Abstract

Diabetes mellitus (DM) is a serious, long-term condition that occurs when raised blood glucose levels persist because the body cannot produce any or adequate insulin or cannot effectively use the insulin it produces. Microvascular complications of DM (which include diabetic nephropathy, diabetic retinopathy, diabetic microangiopathy, and diabetic neuropathy) are mainly associated with vascular permeability impairment that affects different tissues and organs of the body including the kidneys, retina and nerves. This research was aimed to establish the prevalence and associated clinical factors of microvascular complications in patients with type 2 DM in Kano, Nigeria. Total of 410 study participants were recruited using simple random sampling from males and females with type 2 DM attending diabetic clinics at Murtala Specialist Hospital, General Hospital Nasarawa and Aminu Kano Teaching Hospital, Kano. The patients were examined for the presence of any of the diabetic complications using clinical examinations and Laboratory investigations. Microvascular complications were presented as frequencies. The association between the clinical parameters and the microvascular complications was analysed using Chi square analysis. The results show that, out of the total number of 410 study participants, 97 (23.66 %) have Diabetic Retinopathy, 57 (13.90 %) have Diabetic Nephropathy, 59 (14.39 %) have Diabetic Neuropathy, 82 (20.00 %) have multiple Microvascular Complications and 115 (28.05 %) presented with no microvascular complication. There was a significant association between microvascular complications and level of glycaemic control, Physical exercise, Blood pressure, classical signs and symptoms ($p<0.05$). There seem to be no significant association between family history of DM, BMI classes and frequency of microvascular complications of DM. There is a

considerably a moderate prevalence of microvascular complications of DM among the patients with type 2 DM in Kano, Nigeria.
Keyword: *Diabetes Mellitus, Microvascular Complications, Nephropathy, Retinopathy, Neuropathy*

Introduction

Diabetes mellitus (DM) is a serious, long-term (chronic) condition that occurs when raised levels of blood glucose occur because the body cannot produce any or enough of the hormone insulin or cannot effectively use the insulin it produces (1). It is a global pandemic for the 21st century, and subjects with type 2 diabetes can have metabolic and vascular complications. Chronic hyperglycaemia in T2DM is related to microvascular complications (such as diabetic retinopathy, nephropathy, and neuropathy/foot), macrovascular complications (such as coronary heart disease, stroke, and peripheral arterial disease), poor quality of life, and even death (2). Epidemiologic study has shown a fifth of all diabetes patients suffer from two or more micro vascular complications (3). The complications give rise to morbidity and compromise the quality of life for diabetic subjects (4). It is estimated that, the number of people with DM Worldwide as at 2021 was about 537million (1). In Africa alone about 24 million people are diabetic (1). In Nigeria about 3.6 million have diabetes mellitus (1). Incidence of DM is expected to rise, with the projection of 783 million worldwide and 55 million in Africa by 2045 (1). Genetic conditions and environmental factors (including overweight, obesity, and inactivity), and their complex interaction can contribute to development of DM (5). Type 2 diabetes mellitus (T2DM) is a progressive endocrine disease accompanied by a variety of metabolic disorders that manifests clinically as high blood glucose (6). T2DM has swiftly become an urgent health problem because of its associated complications, if left untreated or with no proper care (7). Since chronic hyperglycemia-related damage to small blood vessels results in complications, patients with T2DM with longer disease durations are more likely to develop microvascular complications, such as retinopathy, neuropathy and nephropathy, which will lead to the decline in patients' quality of life, disability and even death (8). Previous studies suggest that a substantial proportion of patients with T2D have already developed diabetes complications such as chronic kidney disease (CKD), at the time of diabetes diagnosis (Bui et al., 2019, An et al., 2021). The disease is characterised by hyperglycaemia caused by impaired insulin secretion or peripheral insulin resistance (10). This trigger counter reactions and activities in which body fats and protein are mobilized to counter the effect of pseudo hypoglycaemia (11). These results into polyphagia, polydipsia and polyuria, with attending nutrient lost and body wastages (11). Chronic systemic complications of DM are of two types: Microvascular and Macrovascular complications. Microvascular complications include diabetic nephropathy, diabetic retinopathy, diabetic microangiopathy, and diabetic neuropathy. Macrovascular complications include cardiovascular disease, heart attacks and stroke (12). People with DM are at significantly increased risk of developing microvascular complications (5). Despite the importance of comorbidities of T2D, there is a lack of evidence describing the natural progression of T2D, the prevalence and the long-term development of diabetes complications over time in a large contemporary cohort of T2D (9). Chronic hyperglycaemia and insulin resistance play a number of important roles in the initiation of the complex biochemical interplay leading to the development of complications of DM uncontrolled hypertension, lack of exercise are among some compounding factors in the development of microvascular complications in DM (13)(14). While previous studies from various countries investigated the prevalence of T2D complications, many of such studies investigated the prevalence of complications cross-sectionally and reported only a limited number of complications, or the timing of prevalence was not specifically at or from the time of T2D diagnosis (9). This research was aimed to establish the prevalence and pattern of the microvascular complications among patients with type 2 DM in Kano, Nigeria.

Materials and Methods

Study Area/Population

This study was conducted at the Department of Medical laboratory Sciences, Faculty of Allied Health Sciences, College of Health Sciences, Bayero University, Kano. The study participants were drawn from the hospital around Kano metropolis (Murtala Specialist Hospital, General Hospital Nasarawa and Aminu Kano Teaching Hospital, Kano). A total of 410 study participants were recruited using simple random sampling from males and females with type 2 DM attending diabetic clinics at Murtala Specialist Hospital, General Hospital Nasarawa and Aminu Kano Teaching Hospital, Kano.

The calculation to determine the sample size was made using Cochran formula (15) as follows.

$n=Z^2P\ (1-P)\ /W^2$

Where, n= desired sample size

P= Prevalence of Retinopathy in diabetic patients 40% (16).

Z= 95% confidence interval=1.96

W= degree of accuracy= 0.05

Therefore

n = 368.7 + 10 % attrition rate = 368.7+36.8793

n = 405.67 approximately 410

Ethical Consideration

Ethical approval for this research was obtained from the Ethics and research Committee of Hospital Services Management Board, Kano State Ministry of Health, Kano. Ethical consideration was in line with Helsinki declaration. A written informed consent was obtained from all the study participants prior to inclusion in the study.

Assessment for Microvascular Complications

From the study participants selected using random Sampling, a questionnaire was served. The patients were examined for the presence of any of the diabetic complications using clinical examinations and Laboratory investigations. Diabetic Nephropathy was diagnosed using Urinary Albumin Creatinine Ratio (ACR). Retinopathy was established by an ophthalmologist and the patients were already receiving care in ophthalmology unit. Neuropathy was established using clinical examination by the presence of symptoms such as pains and use of monofilament examination with the help of physician. The prevalence of the complications determined after all the samples were collected.

Sample Collection

Standard self-administered questionnaire was prepared and administered to all the study participants to obtain their socio-demographic characteristics including, gender, age, tribe, occupation, life style, family history of DM, history of microvascular complications of DM, etc. Four (4) ml of whole blood each was collected from the median cubital vein, using vacuutainer blood collection kits, into the EDTA and Lithium Heparin container. The lithium heparin anti-coagulated blood was centrifuged at 3000 rpm for five minutes to separate the plasma. The separated plasma was transferred in to cryovials and stored at -20^{o} C until used for the analysis of biochemical parameters. The EDTA anticoagulated blood was used for HbA1c analysis. Spot urine was collected into the universal bottle for the determination of urinary Albumin Creatinine Ratio (ACR) and urinalysis. The urinalysis was carried out immediately. The urine sample was aliquot into cryovials and stored at -20^{o} C until used for ACR analysis.

Biochemical and clinical Parameters: Glucose was estimated using Gucometer (Glucose oxidase-peroxidase), HBA1c using Ion exchange chromatography, albumin using

microalbuminuria minikit, Creatinine using Jaffe's method, Blood Pressure was measured using sphygmomanometer, BMI calculated by weight (Kg)/height $(m)^2$.

Data Analysis

The data generated was analysed IBM SPSS statistical software version 25 (Armonk, New York: IBM Corp). The prevalence of microvascular complications were presented as frequencies. The association between the clinical parameters and the microvascular complications was analysed using Chi square analysis. For all analyses, α was set at 0.05/P<0.05 considered significant.

Results

The frequency distribution of microvascular complications viz; Diabetic Retinopathy, Diabetic Nephropathy, Diabetic Neuropathy and those with multiple complications in the study population was presented in Figure 1. The results show that, out of the total number of 410 study participants, 97 (23.66 %) have Diabetic Retinopathy, 57 (13.90 %) have Diabetic Nephropathy, 59 (14.39 %) have Diabetic Neuropathy, 82 (20.00 %) have multiple Microvascular Complications and 115 (28.05 %) presented with no microvascular complication.

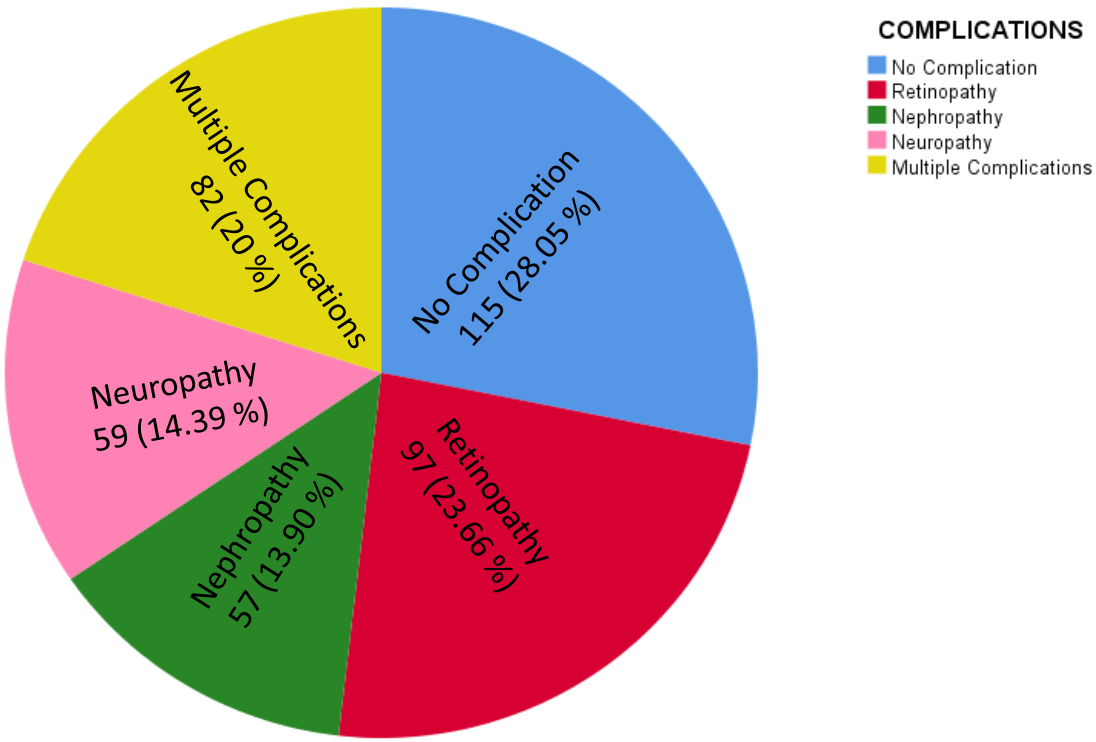

Figure 1: Pie Chart Showing the Frequencies of Microvascular Complications among the Patients with Diabetes Mellitus in Kano, Nigeria. N=410

Table 1: The association between clinical factors and the microvascular complications of DM

Factors		**No Complication**	**Retinopathy**	**Nephropathy**	**Neuropathy**	**Multiple Comp**	χ^2	***P* value**
Glycaemic Control	Good	55(48.3%)	41(41.9%)	11(18.8%)	14(24.1%)	36(44.4%)	20.458	<0.05
	Inadequate	3(2.5%)	11(11.6%)	0(0.0%)	8(13.5%)	14(16.7%)		
	Poor	57(49.2%)	45(46.5%)	46(81.3%)	37(62.5%)	32(38.9%)		
Family History DM	Yes	82(71.0%)	56(57.7%)	26(46.7%)	37(62.5%)	41(50.0%)	0.454	>0.05
	No	33(29.0%)	41(42.3%)	31(53.3%)	22(37.5%)	41(50.0%)		
Routine Exercise	Yes	33(29.0%)	0(0.0%)	8(13.3%)	3(6.3%)	0(0.0%)	16.802	<0.05
	No	82(71.0%)	97(100.0%)	49(86.7%)	56(93.8%)	82(100.0%)		
Classical Signs	Present	89(77.4%)	90(92.3%)	42(73.3%)	48(81.3%)	60(72.7%)	10.648	<0.05
	Absent	26(22.6%)	7(7.7%)	15(26.7%)	11(18.8%)	22(27.3%)		
Blood Pressure	Hypertensive	55(48.4%)	60(61.5%)	42(73.3%)	30(50.8%)	67(81.8%)	9.888	<0.05
	Normotensive	60(51.6%)	37(38.5%)	15(26.7%)	29(49.2%)	15(18.2%)		
BMI	Under weight	7(6.5%)	3(3.5%)	8(13.3%)	0(0.0%)	0(0.0%)	15.533	>0.05
	Normal weight	37(32.3%)	26(26.9%)	8(13.3%)	11(18.8%)	22(27.3%)		
	Over Weight	41(35.5%)	38(38.5%)	22(40.0%)	26(43.8%)	15(18.2%)		
	Class I Obese	22(19.4%)	19(19.5%)	11(20.0%)	18(31.3%)	30(36.4%)		
	Class II Obese	4(3.2%)	11(11.5%)	8(13.3%)	4(6.3%)	11(13.6%)		
	Class III Obese	4(3.2%)	0(0.0%)	0(0.0%)	0(0.0%)	4(4.5%)		

The chi square analysis on the association between the degree of control of glycaemia (Good = HBA1c <7%, Inadequate = HBA1c 7-8%, Poor = HBA1c >8%), Family history of DM, Exercise, Classical signs and symptoms of DM (polyuria, polydipsia, polyphagia), Blood pressure (hypertensive = blood pressure >135/85 mmHg, Normotensive = <135/85), BMI class. *P* value of <0.05 was considered significant

Discussion

In the current study, the frequency of microvascular complications (Diabetic Retinopathy, Diabetic Nephropathy, Diabetic Neuropathy and those with multiple complications) was determined in patients with type 2 DM in Kano. The results showed that (23.66 %) of the patients with type 2 DM in Kano have Diabetic Retinopathy; this is lower than the (35 %) overall prevalence of any retinopathy in persons with DM by IDF, (16). It is, however, higher than the (12%) in the Africa region reported by the regional survey (16). The (23.66 %) found by the current study was similar but slightly higher than the prevalence of (20.5 %) reported by Kyari et al. (170, who surveyed the prevalence and risk factors for DM and diabetic retinopathy from the Nigeria national blindness and visual impairment survey. This prevalence was also lower than the (34 %) reported from the results of a multicenter study of profile of Nigerians with DM who presented with retinopathy (18). It is also lower than the (48.9 %) reported by Olamoyegun et al. (19) who investigated the burden and pattern of micro vascular complications in type 2 diabetes in a tertiary health institution in Nigeria. The reason for this wide difference between the current study and previous findings may be due to compliances in the treatment guidelines for DM as majority of the current study participants attend diabetic clinics regularly and follow their treatment plan and therefore better glycaemic control. Poor glycaemic control facilitates the development and the severity of diabetic complications (20). The prevalence of the current study was however, lower than (9.28 %) reported by Fawwad et al. (4) who assessed the incidence of microvascular complications of type 2 DM in a 12 year longitudinal study from Karachi-Pakistan. It also lower than the (9.5 %) reported by Bansal et al. (13) in a study of microvascular complications and their associated risk factors in newly diagnosed patients with type 2 DM in India. This low prevalence reported compared to the current study may be due to intensive blood glucose control through diet with medication which can prevent the onset of diabetic retinopathy by 76% (16).

The current study found the prevalence of Diabetic Nephropathy in Kano to be (14.39 %) which is lower than the prevalence reported by IDF (16) based on the data from UK and US of (20—40 %), but is in agreement to findings of a recent study which showed that about 12% of patients had CKD at the time of T2D diagnosis, and concluded that the high prevalence of microvascular and macrovascular complications can be a result of hyperglycemia progression even before the clinical diagnosis of diabetes, but organ damage caused by the presence of other comorbidities may also play a role (9). The finding in the current study is, however, much lower than that of Olamoyegun et al.(19) who reported the prevalence of (54.5%) of Diabetic nephropathy from a study of burden and pattern of micro vascular complications in type 2 DM in a tertiary health institution in Nigeria. The difference in this prevalence may be due to a better glycaemic control from the participants of the current study. Also another factor for the big difference between the current study and the previous findings is that, the current study considered each microvascular complications independently; those with co-microvascular complications such as retinopathy and neuropathy in addition to nephropathy were grouped (independently) under multiple complications subgroup.

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The finding of the current study is, however, much lower than the (3.2%) prevalence by (18) who studied the profile of Nigerians with DM and presented a multi-center study. This prevalence of (14.39 %) in this study is, however, similar to the finding of Fawwad et al. (2018), who reported the prevalence of diabetic nephropathy to be (13.02 %) in the study of incidence of microvascular complications of type 2 DM in a 12 year longitudinal study from Karachi-Pakistan.

The current study found the prevalence of Diabetic Neuropathy to be (20.00 %) in Kano which is within the range of the reported prevalence of diabetic peripheral neuropathy of (16%) to as high as (66%) (16). This is in agreement with a multi-ethnic cohort study of adults with T2DM that reported an overall prevalence of 26.71%, for diabetic neuropathy, and that the independent and significant correlates of risk factors include duration of diabetes, poor glycemic control, and history of hypertension, cardiovascular disease and depressive symptoms (21). Bui et al. in another study on prevalence of and factors related to microvascular complications of T2DM in Tianjin province of China reported (23.5%) for diabetic neuropathy, and was the most frequent complication followed by diabetic retinopathy (17.4%) and diabetic nephropathy (10.8%) (8). The prevalence in this study is however, much lower than the (59.2 %) prevalence of diabetic neuropathy reported by Chinenye et al. (2012) who studied the profile of Nigerians with DM and presented a multicenter study in South East, Nigeria. In another study, an overall prevalence of diabetic neuropathy 40.3% was reported, which is slightly higher among males (43%) than females (37%). The study also reported diabetic neuropathy prevalence of 29.1% among patients with T1D and 42.2% for T2D, respectively (22). The prevalence of (20 %) in the current study is higher than the (10.6 %) found from a study of incidence of microvascular complications of type 2 DM in a 12 year longitudinal study from Karachi-Pakistan (4). And 3-4% reported by An, J 2021 in a recent study on Prevalence and incidence of microvascular and macrovascular complications over 15 years (2004 – 2014) among patients with incident type 2 diabetes.

The current study found the prevalence of patients with type 2 DM with Multiple Microvascular Complications to be (28.05 %). In this study, multiple complications have been defined by the patients presenting with more than one microvascular complication as at the time of recruitment. Majority of the patients in this category have neuropathy and other microvascular complications. Previous research did not focus on patients with more multiple complications; each complication was assessed differently and independently.

In this study, there was strong association between the level of glycaemic control and the development of microvascular complications in patients with type 2 DM. this is in agreement with a study by Ramanathan RS., which shows a clear correlation between longer duration, poor glycemic control and hypertension with microvascular complications of diabetes (23) (21). These microvascular complications could lead to visual, renal as well as neurological function impairment including death and also increase the cost to the patient and society. Poor glycaemic control is highly correlated with the development of the complications. Al – Shehiri, in his study

reported high prevalence rates of microvascular complications among type 2 diabetics in Kingdom of Saudi Arabia (mainly retinopathy (45.8%) or neuropathy (32.7%), while the prevalence of nephropathy was 9.9%) which was all attributed to poor glycaemic control (glycosylated haemoglobin (HbA1c) > 8%) (24). Likewise, patients who lack exercise have higher prevalence of the microvascular complications indicating the relationship that exist between the frequency for the development of the complications and lack of exercise. This study also showed that there is a strong association between the blood pressure control and the microvascular complications in type 2 DM. Those with poorly controlled blood pressure have higher prevalence of the complications than the normotensive patients. Presence of classical signs and symptoms of DM (polyuria, polydipsia and polyphagia) was highly associated with the increased incidence of the microvascular complications in this study subject. BMI and family history of DM seemed to have less association with the development of microvascular complications in the study population (25-45).

Among the patients with Type 2 DM in Kano, 23.66 %, this is similar to reports by Al-Shehiri (24) who reported a prevalence of 23.7% for Type 2 DM in Saudi Arabia. The current study also reported a prevalence of 13.90 % diabetic retinopathy, which is in agreement to similar report by Bui *et al.* (8), that reported a prevalence of 17.4%, this study also reported a prevalence of 14.39 % for diabetic Nephropathy, which is slightly higher to reports by Bui, et al. (8) of 10.8%. The current study has Diabetic Neuropathy, 20.00 % have multiple Microvascular Complications and 28.05 % presented with no microvascular complication of DM.

There is need of aggressive screening for early detection of microvascular complications to prevent or retard the progression of complications. Beyond screening, there is need for educating the patients regarding the diabetes related complications to encourage earlier medical consultation.

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