Spectrum of musculoskeletal disorders in Nigerians with types 2 diabetes mellitus: prevalence and predictors

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SUMMARY
Musculoskeletal (MSK) conditions are more frequently found among patients with diabetes mellitus (DM) than in the non-diabetics. Despite several reports outside Africa, they have been under-studied among Africans. This study aimed to assess the overall prevalence and predictors of MSK conditions in Nigerian with types 2 diabetes mellitus (T2DM). A total of 268 adult with T2DM and 268 non-diabetic controls were recruited. All study subjects had their socio-demographics and clinical parameters obtained using interviewer-administered questionnaire. Musculoskeletal conditions among study subjects were classified using validated criteria and case definitions. Musculoskeletal disorders (MSKD) were significantly more frequent amongst subjects with DM (56% vs 22%, OR=4.5 p=0.001), Osteoarthritis (9.3% vs 4.1%, p=0.016), lumbosacral spondylosis (5.6% vs 2.2%, p=0.045), limited joint mobility (13.8% vs 5.6%, p=0.001), adhesive capsulitis (4.5% vs 1.5%, p=0.042) and rotator cuff tendinitis (3.7% vs 0.4%, p=0.006) were more frequent in DM subjects than in controls. Logistic regression showed that age (OR=2.1, CI=1.5-2.6) and waist circumference (OR=3.0, CI=2.6-3.4) are independent predictors of MSKD among patients with diabetes. This study found higher prevalence of MSKD among diabetic subjects. It also identified certain factors associated with MSKD among patients with diabetes mellitus.

Key words: Spectrum, musculoskeletal disorders, Nigerians, types 2 diabetes.

INTRODUCTION
Musculoskeletal disorders (MSKD) in diabetes mellitus (DM) are common and have been shown to be more prevalent than in persons who do not have DM (1-4). They are under-researched and under-reported compared with well-known micro- and macro-vascular disease in DM. The prevalence of DM in the world, particularly in developing countries, has been on an upward trend. The estimated number of adults with DM in Nigeria in year 2010 was 2.8 million with a prevalence of 3.9% while the projection for 2030 is 5.3 million with a prevalence of 4.3% (5). DM is a multisystem disease and the musculoskeletal system is often affected perhaps due to reduced physical activity, obesity and aging. A wide spectrum of MSKD have been described in diabetic patients, and these include limited joint mobility (LJM), carpal tunnel syndrome, DeQuervain’s tendinitis, bicipital tendinitis, adhesive capsulitis, finger flexor tenosynovitis (trigger finger), diffuse idiopathic skeletal hyperostosis (DISH), gout, osteoarthritis and several others (6). Some of these conditions arise directly as a consequence of chronic complications of DM, while others have increased incidence in DM due to epidemiologic associations (7). The exact cause of MSK conditions in DM...
is not known; however, it was suggested that the metabolic disturbances in DM such as glycosylation of proteins, microangiopathy, neuropathy as well as collagen deposition in skin and periarticular structures, may result in changes observed in the connective tissue structures (8). MSKD may occur in DM of short and long term durations, in any type of DM and may even be the presenting features of the disease (9). Rheumatic hand conditions have been identified as harbingers of undiagnosed DM (10). Similarly, co-existence of MSKD with DM may predict subsequent development of microvascular complications, increase hospital utilisations and worsening quality of life (QOL). Rosenbloom et al. (11) found 83% risk of microvascular complications after 16 years of DM in the presence of LJM in comparison with a 25% risk in the absence of LJM. In comparison with persons without DM, diabetic patients had higher 10 year cumulative incidence of MSK pain and hospital visits for MSK pain as well as lower QOL physical component score (12, 13). MSKD of DM have been studied elsewhere with varying scope and different prevalence reports. There is only one published case-control study of limited joint mobility (LJM) among DM patients from Nigeria while the other was a case report (2, 14).

## MATERIALS AND METHODS

The study was conducted at the endocrine clinic of Lagos State University Teaching Hospital (LASUTH), located in Ikeja, the capital city of Lagos, Nigeria. This study is a cross-sectional comparative study that was carried out over a period of six months. Two hundred and sixty eight adult subjects with type 2 DM (T2DM) were recruited using systematic random sampling technique. Same number of control subjects without DM were recruited from the hospital’s member of staff and visiting patient’s relatives. Out of 268 control subjects recruited, hospital staff were 154 in number while patient’s relatives were one hundred and fourteen. The Kish’s formula \( \left( Z^2PQ/D^2 \right) \) for samples size determination in a cross-sectional study was used (15). Sample size was calculated using a tolerable sampling error (D) of 0.05, confidence interval (Z) of 1.96 and prevalence (P) of 19% obtained in a Nigeria study on LJM\(^2\). The sample size was 262 after allowing 10% drop out rate. All patients recruited provided informed consent while diabetic patients with traumatic and congenital MSK conditions, those on steroids and those with co-morbid endocrine diseases were excluded from the study. All control subjects were further screened by random blood glucose test. Controls with impaired glucose tolerance, ‘DM’ range blood glucose and other endocrine diseases were excluded from the study. Approval was granted by the Research Ethics Committee of LASUTH before the commencement of the study and informed and written consent was obtained from the study participants.

(a) Clinical Assessment

The anthropometrics and blood pressure were assessed in all subjects using standard techniques. Musculoskeletal examination included both the general and specific MSK assessments. General inspection of the subjects for abnormal gait, loss of function, joint deformities, subcutaneous nodules and joint swelling was carried out in all subjects. The joints and peri-articular structures were palpated for swelling, effusions, tenderness, crepitus and warmth while active range of motion of the joints was followed by passive joint mobilizations in subjects with limited active joint motion. Resisted active joint motion, provocative joint manoeuvres and some special tests such as Tinel’s and Phalen’s test for carpal tunnel syndrome, Finkelstein’s test for Dequervain’s tendinitis, prayer and table top tests for LJM, were carried out where applicable to identify specific MSK conditions.

(b) Laboratory and radiological assessments

Fasting and random whole blood glucose were measured for cases and controls, respectively, using a glucometer. In addition, two hour post prandial whole blood glucose
and HBA1C measurement were carried out for diabetic cases while venous blood sample was collected for determination of ESR, haematocrit, WBC, SUA, HDL cholesterol, triglycerides and hsCRP in all subjects using standard techniques. All subjects were categorized into two groups of presence and absence of anaemia, hyperuricemia, obesity, abdominal obesity, metabolic syndrome, dyslipidaemia, elevated hsCRP, elevated ESR, leucocytosis, hypertension, reduced HDL, and elevated TG. Plain radiographs of the affected joints were done for patients requiring X-rays for definitive diagnosis and to exclude alternative diagnosis.

MSKD among the patients were diagnosed using the validated ACR endorsed criteria (16) for fibromyalgia (FM), gout and osteoarthritis (OA) of the knee, hip and hand. Southampton examination schedule (17) was used for diagnosis of upper limb MSK such as adhesive capsulitis (AC), rotator cuff tendinitis (RCT), bicipital tendinitis (BT), DeQuervain’s tendinitis (DQT), carpal tunnel syndrome (CTS), lateral epicondylitis (LE) and medial epicondylitis (ME). Operational definitions were adopted for MSK conditions without classification criteria and for some clinical and laboratory parameters.

Operational definitions for diagnosis of some MSK disorders and metabolic abnormalities

1) Flexor tenosynovitis (trigger fingers, TF): Patients having a palpable nodule, usually in the area overlying the MCP joints, and thickening along the affected flexor tendon sheath on the palmar aspect of the finger and hand. The locking phenomenon may be reproduced with either active or passive finger flexion (1).

2) Limited joint mobility (LJM): will be diagnosed by presence of positive ‘prayer sign’ and ‘table top test’.

The “prayer sign,” which tests the ability to flatten the hands together as in prayer, facilitating recognition of contractures (11).

The “table top test,” which assesses the ability to flatten the palm against the surface of a table (11).

3) Plantar fasciitis (PF): heel pain and or plantar heel pain at any time with either plantar heel tenderness or plantar heel pain on passive dorsiflexion of the foot (18).

4) Subacromial bursitis (SB): painful impingement tests on forced passive internal rotation, resisted external rotation and forced passive forward flexion (19).

5) Symptomatic cervical spondylosis (SCS): Mechanical neck pain or stiffness greater than or equal to 3 months supported by typical radiographic features.

6) Symptomatic lumbar spondylosis (SLS): Mechanical low back pain or stiffness greater than or equal to 3 months supported by typical radiographic features.

Statistical analysis

Data obtained were analysed using statistical package for social science (SPSS) version 19. All categorical variables were summarized and presented as frequency and percentages while all quantitative variables were expressed as mean and standard deviation (SD), as well as median and inter-quartile range, where applicable while the differences between the categorical variables were compared using Chi-square tests, the difference between the numerical variables were compared using independent t test. The Mann Whitney U test was used to compare non-parametric numerical variables. Binary logistic regression analysis was performed to determine the categorical and numerical predictors of musculoskeletal conditions among the diabetic subjects. Statistical significance was set at p value <0.05.

RESULTS

Socio-demographic characteristics of the study subjects

Two hundred and seventy six subjects with T2DM were initially recruited for the study, out of which eight cases had no laboratory results, due to insufficient samples. Also, two hundred and eighty one controls were initially recruited but thirteen were exclude due to impaired glucose tolerance and diabetic range blood glucose. The mean ages of the DM cases and control groups
were comparable (59.4±12.7 vs 57.3±12.4 years, t=0.926, p=0.06). Females constituted more than 70% of the subjects in both groups. The occupations of the two groups were comparable (p=0.281) with a significant difference in the level of education between the two groups (p=0.001). Table I shows socio-demographic characteristics of the study subjects.

Prevalence and patterns of musculoskeletal conditions among study subjects

The prevalence of MSK conditions in diabetic group was higher than in the control group (DM-56%, control-22% OR=4.5, p=0.0001). While some MSK conditions such as OA (9.3% vs 4.1%, p=0.016), symptomatic LS (5.6% vs 2.2%, p=0.045), LJM (13.8% vs 5.6%, p=0.001), AC (4.5 vs 1.5, p=0.042) and RCT (3.7% vs 0.4%, p=0.006) were significantly more frequent in DM subjects than in the controls, conditions like BT, gouty arthritis, Dupuytren’s contracture, and ME were not documented in the controls. The comparisons of the prevalence and types of MSKD between DM and control subjects are shown in Table II.

Factors associated with presence of musculoskeletal conditions among subjects with types 2 DM

Categorical variables

Bivariate analysis using Chi-square statistics showed that female sex (OR=2.3, p=0.0007), old age (OR=2, p=0.0007), long standing DM (OR=12.3, p=0.001), lack of formal education (OR=2.1, p=0.004), poor glycemic control (OR=4.8, p=0.001), use of statins (OR=9.8, p=0.001), hyperuricemia (OR=1.8, p=0.024), hypertension (OR=1.8, p=0.029), obesity (OR=1.9, p=0.012), metabolic syndrome (OR=1.8, p=0.028) and low HDL (OR=2.2, p=0.002) were associated with MSKD in DM. Also, poor glycemic control was more frequently observed in DM subjects with MSKD than in the DM subjects without MSKD.

Numerical variables

The median age was significantly higher among DM subjects with MSKD (65 years (58-70 years) vs 61 years (50.8-68 years), p=0.026). Similarly, the median duration of

Table I - Socio-demographic characteristics of subjects with diabetes and controls.

| Variables     | DM subjects (N=268) n (%) | Controls (N=268) n (%) | p value |
|---------------|---------------------------|------------------------|---------|
| Sex           |                           |                        |         |
| Male          | 53 (19.8)                 | 60 (22.4)              | 0.459   |
| Female        | 215 (80.2)                | 208 (77.6)             |         |
| Occupation    |                           |                        |         |
| Traders       | 133 (49.6)                | 110 (41)               | 0.281   |
| Office workers| 71 (26.5)                 | 95 (35.4)              |         |
| Artisans      | 29 (10.8)                 | 26 (9.7)               |         |
| Manual workers| 18 (6.7)                  | 25 (7.8)               |         |
| Students      | 5 (1.8)                   | 6 (2.2)                |         |
| Others        | 12 (4.5)                  | 10 (3.7)               |         |
| Education     |                           |                        |         |
| Primary education | 77 (28.7)             | 79 (29.5)             | 0.001   |
| Secondary education | 62 (23.2)             | 51 (19.0)             |         |
| Tertiary Education | 28 (10.4)            | 108 (40.3)            |         |
| Not Educated  | 101 (37.7)                | 30 (11.2)              |         |

Key: DM=diabetes, n= frequency of each variable, N=Total number of subjects in each group, %= proportion of each variable.
DM was significantly higher among DM cases with MSKD (12 years (10-15 years) vs 7.8 years (4-12 years). The DM subjects with MSKD had higher mean BMI, HbA1C, HDL-c and waist circumference. The comparisons of clinical, anthropometric, haematological and biochemical variables between the groups are shown in Tables III and IV.

**Predictors of MSKD among subjects with types 2 DM**

Further analysis of significant variables obtained from bivariate statistics with binary logistic regression showed that age (OR=2.1, CI=1.5-2.6) and waist circumference (OR=3.0, CI=2.6-3.4) are predictors of MSK conditions among types 2 DM subjects.

**DISCUSSION**

This present study is consistent with previous reports of higher prevalence of MSK conditions among subjects with T2DM as it demonstrates that they are 2.5 times more frequent in persons with DM (20-25). This difference is significant such that persons with DM have 4.5 times greater odds of developing MSKD. The reported prevalence of MSKD among diabetic patients varies widely depending on DM populations whether type 2 only, type 1 only or mixed, as well as the case definitions of MSK systems studied. Our finding is comparable to prevalence of 54% documented among Indian T2DM patients (26). However it is much higher than the prevalence of 42.58% by Ashishi et al. (1), 13.3% by Kidwal et al. (23) and 33.3% by Bhat et al. (21). The higher proportion of elderly patients in our series may explain in part the discrepancy between our prevalence result and others reported elsewhere. Three reports from Africa were from mixed DM populations (27-29). Their results showed that MSK conditions were more common in type 2 DM subjects than in type 1 subjects (Morocco)
type 2 DM 37.4% vs type 1 DM 17.2%,
Egypt (28)-type 2 DM 37%, type 1DM 29%, Ethiopia (29) - type 2 DM 21.3% vs
type 1 DM 10%). It is thought that it may
be explained by the propensity for type 2
subjects to develop MSKD as a result of
obesity, reduced physical activity, older
age, dyslipidaemia, and hyperuricemia.
The prevalence of specific musculoskel-
etal conditions varies across various stud-
ies. Osteoarthritis was the most common
MSKD recorded among T2DM subjects
in studies from Greece (30), Morocco (27)
and India (1). Conversely, studies from
Egypt (28), Pakistan (23), and USA (3)
found adhesive capsulitis as the most fre-
quent MSKD. The most frequent MSKD
observed among DM subjects in the present
study was limited joint mobility, followed
closely by symptomatic osteoarthritis. This
finding is in keeping with the report by Ray
et al. (30), who documented limited joint
mobility as the commonest MSKD among
diabetic subjects. The differences may be
attributed to scopes of MSKD studied as
well as different case definitions used by
various investigators.
Musculoskeletal conditions were more fre-
frequent in the female diabetics. This finding
is in keeping with previous studies among
Africans and non-Africans (2, 3, 29). This
observation also mirrors the higher preva-
lence of MSKD among females than males
in the general population (31). On the con-
trary, a study from India reported equal dis-
tribution of MSKD between male and fe-
male DM patients (1). While middle aged
and elderly persons in the general popu-
lation often have high frequency of MSK
conditions due to age related degeneration
of articular cartilage and peri-articular
structures, this risk was found to increase
in the presence of DM, (22, 32). In this
study, the proportion of elderly DM sub-
jects with MSK conditions was significant-
ly higher than elderly DM subjects without

| Variables | DM Cases with MSS conditions n (%) n=150 | DM cases without MSS conditions n (%) n=118 | Odds ratio | Confidence interval | P-value |
|-----------|------------------------------------------|---------------------------------------------|------------|---------------------|---------|
| Sex       |                                          |                                             |            |                     |         |
| Male      | 21 (14.0)                                | 32 (27.2)                                   | 2.3        | 1.2-4.2             | 0.007   |
| Female    | 129 (86.0)                               | 86 (72.8)                                   |            |                     |         |
| Elderly   | 109 (72.7)                               | 67 (56.8)                                   | 2.0        | 1.2-3.4             | 0.007   |
| No formal education | 68 (45.3) | 33 (28)                                   | 2.1        | 1.3-3.6             | 0.004   |
| Long term DM (>10 years) | 132 (88.0) | 44 (37.3) | 12.3 | 6.6-22.9 | 0.001 |
| Co-morbidity | 85 (56.7) | 53 (44.9) | 1.6 | 0.9-2.6 | 0.056 |
| Poor glycemic control | 127 (84.7) | 63 (53.4) | 4.8 | 2.7-8.5 | 0.001 |
| Use statins | 142 (94.7) | 76 (64.4) | 9.8 | 4.3-21.9 | 0.001 |
| Smoking history | 4 (2.7%) | 3 (2.6) | 0.96 | 0.21-4.4 | 0.950 |
| Alcohol history | 51 (34) | 42 (35.6) | 0.9 | 0.6-1.5 | 0.786 |
| Metabolic syndrome | 107 (71.3) | 69 (58.5) | 1.8 | 1.1-2.9 | 0.028 |
| Hypertension | 118 (77.3) | 77 (65.2) | 1.8 | 1.1-3.1 | 0.029 |
| Hyperuricemia | 78 (52) | 45 (38.1) | 1.8 | 1.1-2.9 | 0.024 |
| Obesity | 83 (55.3) | 47 (39.8) | 1.9 | 1.1-3.1 | 0.012 |
| Abdominal obesity | 89 (59.3) | 69 (58.5) | 1.0 | 0.6-1.7 | 0.887 |
| Reduced HDLc | 107 (71.3) | 62 (52.5) | 2.2 | 1.4-3.7 | 0.002 |
| Elevated TG | 78 (52) | 54 (45.8) | 1.3 | 0.8-2.1 | 0.311 |
| Elevated CRP | 67 (44.7) | 48 (40.7) | 0.94 | 0.56-1.57 | 0.513 |
| Elevated ESR | 28 (18.7) | 20 (16.9) | 1.1 | 0.6-2.1 | 0.716 |
| Anemia | 7 (4.7) | 4 (3.4) | 1.4 | 0.4-4.9 | 0.601 |
| Leukocytosis | 28 (18.7) | 21 (17.8) | 0.96 | 0.541-1.79 | 0.855 |

DM = diabetes, n = frequency of each variable, N = Total number of cases in each group, % = proportion of each variable, HDLc = high density lipoprotein cholesterol, TG = triglycerides, CRP = C-reactive protein, ESR = erythrocytes sedimentation, BMI = body mass index.
MSK conditions. This finding differs from a report in USA by Cheng et al. (25), who observed that young diabetic subjects (18-44 years) had higher prevalence of MSKD compared with the elderly group (22.7% vs 7.2%). The majority of our subjects with DM had no formal education and lack of formal education was more common in DM subjects with MSK conditions than in DM subjects without MSK conditions. Ashish et al. (1) in India also documented that DM cases with MSK conditions had lower level of education than DM cases without MSK conditions. Nigerian diabetics with higher educational exposure may adhere more strictly to healthy lifestyle measures, regular drug therapy and regular clinic visits than those with low or no education, thus translating to fewer complications.

Although, there have been inconsistent relationship between poor glycaemic control and MSK manifestations in DM in the literature, we found in bivariate analysis, an association between poor glycemic control and MSK conditions in DM. This result contrasts with reports from USA (3) and Scotland (37) that found no significant as-

Table IV - Comparisons of clinical, anthropometric, haematological and biochemical variables between diabetic patients with and without MSKD.

| Variables    | DM Cases with MSKD Mean (SD) n=150 | DM cases without MSKD Mean (SD) n=118 | T-tests | P-value |
|--------------|-----------------------------------|--------------------------------------|---------|----------|
| Age          | 65 (58-70)                         | 61 (50.8-68)                         | MWU     | 0.026    |
| Duration of DM| 12 (10-15)                         | 7.8 (4-12)                           | MWU     | 0.001    |
| BMI (kg/m²)  | 29.9±5.3                           | 28.4±5.0                             | 2.311   | 0.022    |
| WC (cm)      | 90.7±11.8                          | 87.1±11.9                            | -2.490  | 0.013    |
| HDLc (mg)    | 60.0±20.0                          | 52.4±23                              | 2.911   | 0.004    |
| TG (mg)      | 164.7 (86.6-372.4)                 | 124.9 (85-276.9)                     | MWU     | 0.122    |
| SUA (mg/dL)  | 6.2 (4.4-7.9)                      | 5.4 (4.1-7.0)                        | MWU     | 0.176    |
| ESR (mm/hr)  | 20 (10-35)*                        | 28 (14.8-45)*                        | MWU     | 0.042    |
| CRP (mg/dL)  | 2.6 (1.5-8.0)*                     | 2.1 (1.3-7.6)*                       | MWU     | 0.304    |
| WBC(10⁹)     | 6.7±2.5                            | 6.8±1.8                              | 0.397   | 0.691    |
| PCV (%)      | 39 (35-51)*                        | 39 (25-54)*                          | MWU     | 0.606    |
| FBS (mg/dL)  | 128 (58-485)*                      | 128.5 (58-429)*                      | MWU     | 0.745    |
| 2HRPP (mg/dL)| 172 (70-482)*                      | 166.5 (72-459)*                      | MWU     | 0.623    |
| HBA1C (%)    | 8.9±2.5                            | 7.7±2.5                              | -3.480  | 0.001    |

Key: Mann-Whitney U test (MWU) for skewed data,* Median (interquartile range) for skewed data, BMI=body mass index, WC-waist circumference, HDLc= high density lipoprotein cholesterol, TG= triglycerides, CRP- c-reactive protein, ESR=erythrocytes sedimentation rates, SUA=serum uric acid, PCV=packed cell volume, WBC=white blood cells, FBS= fasting blood glucose, 2HRPP=2 hour post prandial, HBA1C=glycated haemoglobin.
association between poor glycemic control and MSKD. However, it is in tandem with the reports among Arabs (38). Similarly, we found an association between DM duration and MSKD. Evidence has shown that prolonged hyperglycaemia causes glycosylation of proteins, microvascular abnormalities, and collagen accumulation in skin and periarticular structures. This results in changes in the connective tissue, and subsequent development of articular and periarticular diseases among diabetics (8).

The predictors of MSKD in DM vary across studies and the relationships of most of these predictors with MSKD have not been consistent. Among Ethiopians, sex, type of DM, and age were independent predictors of MSK conditions (29). Furthermore, previous studies (1, 3) have documented significant association of hypertension, comorbidity, waist circumference, and duration of T2DM with presence of MSK manifestations among DM subjects. Despite the results of bivariate analysis from this study showing strong association between some variables and MSK conditions, further test of these variables in multivariate analysis revealed that only age and waist circumference were predictors of MSK conditions. The heterogeneity in methodology, sample size and study objectives adopted by different investigators may be the explanation for this disparity.

Musculoskeletal ultrasound and MRI would have increased diagnostic precision for soft tissue rheumatic conditions in this study but were not done in our subjects as diagnosis was mostly clinical.

**CONCLUSIONS**

Similar to previous reports, this study documented significantly higher prevalence of MSK conditions among diabetic subjects compared with the non-diabetic controls. It also identified certain factors associated with the presence of MSK conditions among persons with DM. Large prospective cohort studies will offer higher quality of evidence to answer if truly DM or poor glycemic control is a risk factor for MSKD in DM. We suggest that screening for MSK conditions should be an integral part of DM care plan.

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