e-ISSN: 0975-1556, p-ISSN:2820-2643

Available online on www.ijpcr.com

International Journal of Pharmaceutical and Clinical Research 2023; 15(1); 1006-1014
Original Research Article

# A Study on Musculoskeletal Manifestation of Type 2 Diabetes Mellitus and its Association with Markers of Disease Progression

**Medha Gupta[1], Kishore Moolrajani[2], Dharam Prakash Bansal[3], Puneet Rijhwani[4], Ram Kishan Jat[5], Namrata Pareek[6]**

[1]Third Year Resident, Dept of General Medicine, MGMCH, Jaipur
[2]Professor & Unit Head, Dept of General Medicine, MGMCH, Jaipur
[3]Professor & Unit Head, Dept of General Medicine, MGMCH, Jaipur
[4]Professor & Hod, Dept of General Medicine, MGMCH, Jaipur
[5]Associate Professor, Dept of General Medicine, MGMCH, Jaipur
[6]Assistant Professor, Dept of General Medicine, MGMCH, Jaipur

**Received: 25-11-2022 / Revised: 25-12-2022 / Accepted: 30-01-2023**
**Corresponding author: Dr. Puneet Rijhwani**
**Conflict of interest: Nil**

**Background:** Diabetes is one of the top 10 causes of death globally. Diabetes mellitus accounts for a number of vascular complications, which impairs patients' survival. Musculoskeletal complications are also found, and, although less valued than the vascular ones, they significantly compromise the patients' quality of life. This study tries to find out the musculoskeletal manifestation of type 2 Diabetes Mellitus and its association with markers of disease progression.

**Methods:** A Hospital based Observational study was conducted in in the Department of Medicine Mahatma Gandhi Medical College Hospital, Jaipur from the period of March 2021 to September 2022 among 100 patients of type 2 diabetes mellitus, with Fasting Blood sugar levels ≥126 mg/dl and Glycated HBA1C levels ≥ 6.5 were selected and associated musculoskeletal disorders were noted.

**Results:** Majority of study subject i.e., 24% had Cheiroarthropathy. Among 29 patients with HbA1c level <7%, 31% had deformity; among 49 patients with HbA1c level 7-10%, 91.8% had deformity while among 22 patients with HbA1c level>10%, 81.8% had deformity ($p<0.0001$). In 1st tertile of CRP out of 33 patients 17 patients developed Musculoskeletal deformity, in tertile 2 out of 34 patients 25 patients developed muscular deformity while in tertile 3 out of 33 patients 30 patients developed muscular deformity.($p<0.0001$).

**Conclusion:** As CRP is an established marker of inflammation and also cardiovascular disease marker, and HbA1c a marker of disease progression it is important to estimate the CRP and HbA1c levels and this study found musculoskeletal disorder significantly associated with increased HbA1c and CRP level in the patient of Type 2DM.

**Keywords:** Type 2 DM, Hba1c, Inflammation, Vascular Complications.

## Introduction

Diabetes mellitus (DM) is a chronic metabolic disease of high prevalence, [1] which has become a public health problem. In 1985, the world prevalence of DM was approximately 30 million cases, which increased to 177 million in 2000.2 Based on current tendencies, more than 360 million individuals will have the disease by 2030. [2]

Diabetes mellitus accounts for a number of vascular complications, which impairs patients' survival. Musculoskeletal complications are also found, and, although less valued than the vascular ones, they significantly compromise the patients' quality of life. Recent data show that the prevalence of Musculoskeletal manifestations in the hands and shoulders in patients with type 1 or type 2 diabetes is 30 %. [3]

Recently, many studies have proved that inflammation plays an important role in the occurrence of arteriosclerosis and cardiovascular diseases. CRP levels are higher in people with diabetes compared with those without diabetes. [4] So, the purpose of the study to found out the association of Musculoskeletal Manifestations in Type 2 diabetic patients With HBA1C, CRP And Duration of Diabetes in our tertiary center hospital.

## Review Of Literature

Diabetes is one of the top 10 causes of death globally. Together with cardiovascular disease, cancer and respiratory disease, these conditions account for over 80% of all premature non- communicable diseases (NCDs) deaths. [5] Presence of diabetes is associated with increased mortality from infections, cardiovascular disease, stroke, chronic kidney disease, chronic liver disease, and cancer. [6] It has been shown that Asians have higher incidence rates as compared to White American population [7].

Musculoskeletal disorder like Diabetic Cheiroarthropathy, or "stiff-hand syndrome" is characterized by painless limitation of mobility of the small joints of the hands. The prevalence ranges from 8% to 50% among patients with diabetes, compared with only 4% to 20% among individuals without DM [8] Other disorder include Trigger finger (stenosing flexor tenosynovitis), Adhesive capsulitis (frozen shoulder), Neuropathic arthritis (Charcot joints, diabetic osteoarthropathy) etc.

Glycated haemoglobin (HbA1c) which indicates in blood glucose levels during the previous two to three months correlates well with the risk of long-term diabetes complications [9] Non diabetes, prediabetes and diabetics usually falls within the 4.0%–5.6% HbA1c range, 5.7%–6.4% and 6.4% or higher respectively.

In healthy young adult volunteer blood donors, the median concentration of CRP is 0.8 mg/l, the 90th centile is 3.0 mg/l, and the 99th centile is 10 mg/l [10], but, following an acute-phase stimulus, values may increase from less than 50 μg/l to more than 500 mg/l, that is, 10,000-fold.

## Aim & Objectives

- To study Musculoskeletal manifestations in type 2 Diabetes Mellitus and their relative frequency.
- To study association between musculoskeletal manifestations and **markers of disease progression**

## Materials & Methods

**Place of study:** The proposed study was conducted in the Department of Medicine Mahatma Gandhi Medical College & Hospital, Jaipur

**Study Design:** A Hospital based Observational study was planned.

**Study Period:** From the period of March 2021 to September 2022.

**Sampling technique and study population:** A total of 100 patients of type 2 diabetes mellitus, with Fasting Blood sugar levels ≥126 mg/dl and Glycated HBA1C levels ≥ 6.5 were selected as cases using ion exchange chromatography techniques. Musculoskeletal complications assessments were done by clinical examinations, X-ray and CT scan/MRI. Blood samples collected from the cases to measure the serum CRP levels and other routine tests, EDTA sample collected for HBA1C.

Association between duration of Diabetes Mellitus, musculoskeletal complications with HBA1C and CRP levels was studied. A random selection of subjects for the study was made on basis of detailed history and proper clinical examination and with above given test and with following inclusion and exclusion criteria:

**Inclusion Criteria:**

- Confirmed cases of Type 2 Diabetes Mellitus
- Musculoskeletal Manifestations
- Trigger Finger
- Frozen Shoulder
- Carpal Tunnel Syndrome
- Diabetic Cheiroarthropathy
- Charcot's Neuroarthropathy
- Willing to participate in the study.

**Exclusion criteria:**

Patients with the following conditions:

- Patients age <18 years
- Type 1 Diabetes Mellitus
- Patients with Rheumatoid Disease
- Microcrystalline and Metabolic Arthritis
- Patients with Collagen Vascular Disorder
- Patients with history of trauma related to musculoskeletal manifestations.

**Results**

In our study we included 100 diabetic patients out of which 45 were male and 55 were female (ratio 9:11). It shows incidence of diabetes was more in female in comparison to males.

**Table 1: Frequency distribution of Musculoskeletal deformities (n=100)**

| Deformities | Yes | No | Frequency (%) |
|---|---|---|---|
| Trigger Finger (Yes) | 12 | 88 | 12 |
| Frozen shoulder (Yes) | 22 | 78 | 22 |
| Carpel tunnel syndrome (Yes) | 13 | 87 | 13 |
| Cheiroarthropathy (Yes) | 24 | 76 | 24 |
| Charcot's neuropathy (Yes) | 10 | 90 | 10 |

Above table shows out of 100 patients of diabetes 12 % had Trigger finger, 22% had Frozen shoulder, 13% had carpel tunnel syndrome, 24% had Cheiroarthropathy and 10 % patients had Charcot's neuropathy.

**Table 2: Distribution on the basis of HbA1c and CRP (n=100)**

| HbA1c (%) | (n) | Percentage (%) |
|---|---|---|
| <7 | 29 | 29 |
| 7-10 | 49 | 49 |
| > 10 | 22 | 22 |
| | | |
| CRP Tertiles | (n) | Percentage (%) |
| I | 33 | 33 |
| II | 34 | 34 |
| III | 33 | 33 |

29 patients had HbA1c levels <7%, 49 patients had HbA1c levels between 7-10% while 22 patients had >10% HbA1c. 1st tertile of CRP includes 33 patients, 2nd tertile includes 34 patients while 3rd tertile includes 33 patients.

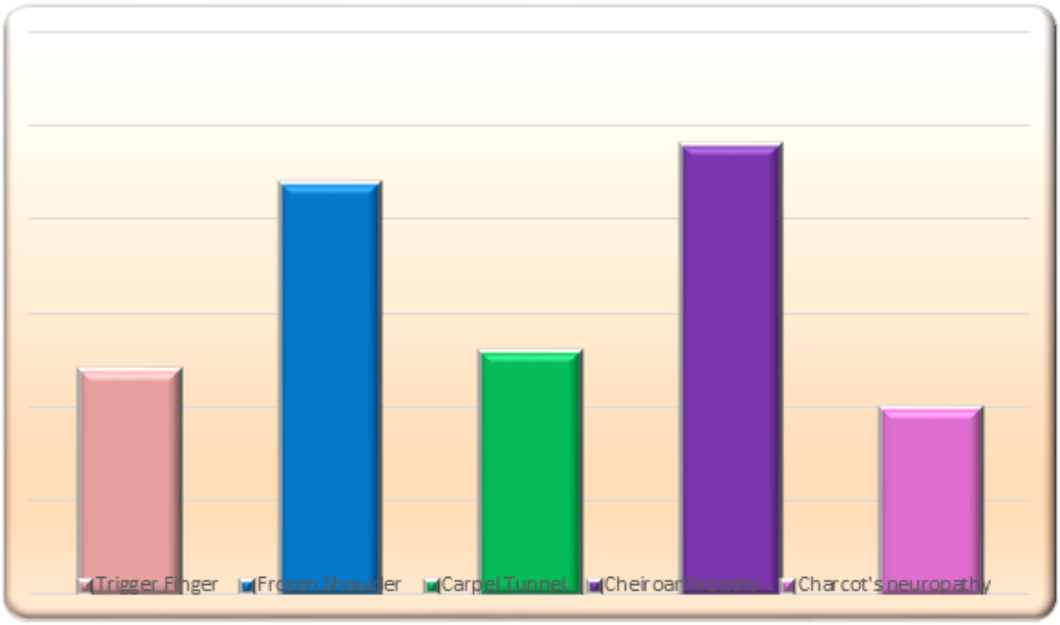


**Figure 1: Frequency distribution of Musculoskeletal deformities**

**Table 3: Musculoskeletal deformities on the basis of HbA1c (n=100)**

| **Deformities** | **HbA1c < 7% n=29** | **HbA1c 7-10% n=49** | **HbA1c > 10% n=22** | **$X^2$** | **P** |
|---|---|---|---|---|---|
| Yes | 09 (31.0) | 45 (91.8) | 18 (81.8) | 107.78 | **<0.0001** |
| No | 20 (68.9) | 04 (8.2) | 04 (18.2) | | |
| | | | | | |
| **Deformities** | **Duration < 5 yrs (29)** | **Duration 5-10 yrs (39)** | **Duration > 10 yrs (32)** | **$X^2$** | **P** |
| Yes | 05 (17.2) | 35 (89.7) | 32 (100) | 187.98 | **<0.0001** |
| No | 24 (82.8) | 04 (10.3) | 00 (00) | | |
| | | | | | |
| **Deformities** | **CRP Tertile I (n=33)** | **CRP Tertile II (n=34)** | **CRP Tertile III (n=33)** | **$X^2$** | **P** |
| Yes | 17 (51.5) | 25 (73.5) | 30 (90.9) | 44.994 | **<0.0001** |
| No | 16 (48.5) | 09 (26.5) | 03 (9.1) | | |

Among 29 patients with HbA1c level <7% 9 patients (31% ) had deformity; among 49 patients with HbA1c level 7-10% 45 patients (91.8%) had deformity while among 22 patients with HbA1c level >10% 18 patients (81.8%) had deformity. This difference was statistically significant (<0.0001)

Among 29 patients with duration of diabetes < 5 years 17.2% (5) had musculoskeletal deformity, among 39 patients with diabetes duration 5-10 years, 35 patients 89.7% (35) had musculoskeletal deformity while among 32 patients with diabetes duration >10 years all of them developed musculoskeletal deformity. This difference was statistically significant (<0.0001)

Above table shows in 1st tertile of CRP out of 33 patients 17 patients developed Musculoskeletal deformity, in tertile 2 out of 34 patients 25 patients developed

muscular deformity, while in tertile 3 out of 33 patients 30 patients developed muscular deformity. This difference was statistically significant (p<0.0001).

**Table 4: Frequency distribution of Musculoskeletal deformities on the basis of HbA1c (N=100)**

| Deformities | HbA1c < 7% n=29 | HbA1c 7-10% n=49 | HbA1c > 10% n=22 |
|---|---|---|---|
| Trigger Finger (Yes) | 01 (3.5) | 07 (14.3) | 04 (18.2) |
| Frozen shoulder (Yes) | 04 (12.8) | 14 (28.6) | 04 (18.2) |
| Carpel tunnel syndrome (Yes) | 01 (3.5) | 10 (20.4) | 02 (9.0) |
| Cheiroarthropathy (Yes) | 04 (12.8) | 12 (24.4) | 08 (36.4) |
| Charcot's neuropathy (Yes) | 00 (00) | 09 (18.4) | 01 (4.5) |

As depicted among those with HbA1c > 10% majority i.e., 36.4% (8) had Cheiroarthropathy, among those with HbA1c 7-10% majority i.e., 28.6% (14) had frozen shoulder and among those with HbA1c <7 % majority i.e., 12.8% (4) had Cheiroarthropathy and frozen shoulder.

**Table 5: Frequency distribution of Musculoskeletal deformities on the basis of Duration of disease (N=100)**

| Deformities | Duration < 5 yrs (29) | Duration 5-10 yrs (39) | Duration > 10 yrs(32) |
|---|---|---|---|
| Trigger Finger (Yes) | 00 (00) | 07 (17.9) | 05 (15.6) |
| Frozen shoulder (Yes) | 1 (3.5) | 10 (25.6) | 11 (34.3) |
| Carpel tunnel syndrome (Yes) | 01 (3.5) | 06 (15.4) | 06 (18.8) |
| Cheiroarthropathy (Yes) | 3 (10.3) | 10 (25.6) | 11 (34.3) |
| Charcot's neuropathy (Yes) | 00 (00) | 04 (10.3) | 06 (18.8) |

As depicted, those with duration of diabetes >10 years and 5-10 years majority i.e., 34.3% (11) and 25.6 % (10) had frozen shoulder and Cheiroarthropathy

## Discussion

The most commonly found endocrine arthropathies are Musculoskeletal (MSK) complications of Diabetes Mellitus, it affects the musculoskeletal system in a number of ways. Metabolic perturbations in diabetes (including glycosylation of proteins; microvascular abnormalities with damage to blood vessels and nerves; and collagen accumulation in skin and periarticular structures) result in changes in the connective tissue.

Musculoskeletal complications are most commonly seen in patients with longstanding duration of type 1 diabetes, but they are also seen in patients with type 2 diabetes. Rheumatological manifestations lead to considerable morbidity.

Recent data show that the prevalence of MSK manifestations in the hands and shoulders in patients with type 1 or type 2 diabetes is 30 %. [11] These manifestations are closely linked to prolonged disease duration [12] and vascular complications. CRP is a well-known inflammatory marker which increases in the inflammatory conditions. Musculoskeletal diseases are inflammatory condition in which CRP may be affected.

So, we planned a study to estimate the musculoskeletal manifestations and their association with markers of disease progression like HbA1c

In our study out of 100 patients, 45 were male and 55 were female (M:F 9:11) showing diabetes more in female in comparison to males. Similar findings

were depicted by study by DANA E et al [13]

In our study Cheiroarthropathy (24%) was the most common musculoskeletal deformity followed by frozen shoulder (22%), Carpel tunnel syndrome (13%), Trigger finger (12%), and Charcot's neuropathy (10%).

According to a study by A. Majjad et al [14] in 2018 the frequency of Musculoskeletal disorders in DM was 34.4% with OA being most common followed by shoulder capsulitis, frozen shoulder, trigger finger and Dupuytren's contracture. Another study conducted by Tariq Ahmed Bhat et al [15] in 2016; they found Osteoarthritis was present in a significant number of their patients with adhesive capsulitis in 13.1%, flexor tenosynovitis in 18.8% and cheiroarthropathy in 17.8% patients

In our study, out of 100 patients of diabetes, 29 patients had HbA1c levels <7% (mean 6.73 $\pm$ 0.18%), 49 patients had HbA1c levels between 7-10% (mean 8.22$\pm$ 0.77%), while 22 patients had >10% HbA1c (mean 11.18$\pm$ 0.83%). This shows maximum patients (49%) had HbA1c levels between 7-10% in our study. [16]

In our study, (n=29) 9 patients with HbA1c level <7%, had musculoskeletal deformities, 4 had frozen shoulder, 1 patient had Carpel tunnel syndrome, 4 patients develop Cheiroarthropathy and 1 had trigger finger and frozen shoulder both.

In our study, (n=49) 45 patients with HbA1c level 7-10% had musculoskeletal deformities; out of these, 6 had trigger finger, 12 had frozen shoulder, 8 patients had Carpel tunnel syndrome, 9 patients had Cheiroarthropathy and 7 patients had Charcot's neuropathy. In our study, (n = 22) 18 patients with HbA1c level>10% had musculoskeletal deformity. Out of them 4 had trigger finger, 4 had frozen shoulder, 2 patients develop Carpel tunnel syndrome, 7 patients develop Cheiroarthropathy and 1 patient had Charcot's neuropathy and Cheiroarthropathy both.

Similar study conducted by A. Majjad et al[14] in 2018 found that in patients with HbA1c (%) < 7, 6 (7.2%) had hand disorders, 9 (10.8%) had shoulder capsulitis, 11(13.3%) had osteoarthritis, 18 (21.7%) MS disorders. While 48 (16.4%) patients with HbA1c levels ≥ 7 had hand disorders, 38 (13%) had shoulder capsulitis, 62(21.2%) had osteoarthritis, 111(37.9%) had MS disorders total. This shows significantly high levels of MS disorders in patients with HbA1c levels >7% in comparison to HbA1c levels <7%.

In our study patients (n=29) with duration of diabetes <5 years, 5 (17.2%) patients had musculoskeletal deformity, with diabetes duration 5-10 years (n=39) 35 (89.7%) patients while 32 (100%) patients with diabetes duration >10 years (n=32) had musculoskeletal deformity. This difference was statistically significant (<0.0001)

In our study we found in patients (n=29) with duration of diabetes <5 years, 1 had frozen shoulder, 1 patient had Carpel tunnel syndrome, 3 patients had Cheiroarthropathy. In our study patients (n=39) with duration of diabetes 5-10 years, 7 had trigger finger, 9 had frozen shoulder, 6 patients had Carpel tunnel syndrome, 9 patients had Cheiroarthropathy and 2 patients had Charcot's neuropathy alone while 1 patient had Frozen shoulder and Charcot's neuropathy both and 1 patient had Cheiroarthropathy and Charcot's neuropathy both. In our study patients (n=32) with duration of diabetes >10 years, 25 patients had single deformity while 7 patients had multiple (mostly 2) deformities.

Similar study conducted by A. Majjad et al[259] in 2018 found 20(9.9%) patients with Diabetic duration <10 years had Hand disorders, 23(11.4%) had shoulder

capsulitis, 29(14.4%) had osteoarthritis, 53(26.2%) MS disorders total. While 34(19.5%) patients with Diabetic duration ≥10 years had hand disorders, 24(13.8%) had shoulder capsulitis, 44(25.3%) had osteoarthritis, 76(43.7%) had MS disorders total. This shows significantly high levels of MS disorders in patients with Diabetic duration ≥10 years in comparison Diabetic duration <10 years.

Similar study by Lee-Wen Pai et al [272] in 2015 found that the 10-year cumulative incidence of musculoskeletal pain and the mean number of doctor visits for musculoskeletal pain were higher in chronic patients (>10 years) of diabetes. Visits increases with duration of diabetes.

In our study 1st tertile (n=33) of CRP, 17 (51.5%) patients had Musculoskeletal deformity, in 2nd tertile (n=34) 25 (73.5%) patients had muscular deformity while in 3rd tertile (n=33) 30 (90.9%) patients had muscular deformity. It shows increase incidence of musculoskeletal deformity with higher tertile or increased CRP levels. This difference was statistically significant($p<0.0001$).

In our study 1st tertile of CRP (n= 33), 17 (51.5%) patients had musculoskeletal deformity. 15 (45.5%) patients had single musculoskeletal deformity while 2 (6%) patients had multiple deformities. 1 patient had trigger finger, 7 had frozen shoulder, 1 patient had Carpel tunnel syndrome, 5 patients had Cheiroarthropathy and 1 patient had Charcot's neuropathy. while 1 patient had frozen shoulder and carpel tunnel syndrome both and 1 patient had Cheiroarthropathy and Charcot's neuropathy both.

In our study in 2nd tertile of CRP (n=34), 25 (73.52%) patients had musculoskeletal deformities; 22 (64.70%) had single deformity while 3 (8.82 %) patients had 2 types of deformity. 4 had trigger finger, 6 had frozen shoulder, 3 patients had Carpel tunnel syndrome, 6 patients had Cheiroarthropathy etc.

In our study in 3rd tertile of CRP (n=33), 30 (90.9%) patients were affected by musculoskeletal disorders; 3 (9.09%) patients had 2 types (multiple) of musculoskeletal disorders; rest 27 (81.81%) had single type of musculoskeletal disorder. 5 patients had trigger finger, 4 had frozen shoulder, 7 patients had Carpel tunnel syndrome etc.

**Summary -**

Diabetes mellitus (DM) is a multi-system disease characterized by persistent hyperglycaemia with which musculoskeletal sequelae of DM are common. So, our aim of this study was to estimate the Musculoskeletal Manifestations in type 2 Diabetes Mellitus and their association with markers of disease progression like HbA1c, CRP etc.

In our study we found Cheiroarthropathy (24%) as most common musculoskeletal deformity associated with diabetes followed by Frozen shoulder (22%). 29 patients had HbA1c levels <7%, 49 had HbA1c levels between 7-10% and remaining 22 had HbA1c levels >10 %. Mean HbA1c for all 3 groups were 6.73 $\pm$ 0.18%, 8.22$\pm$ 0.77%, 11.18$\pm$ 0.83% respectively. CRP levels for all 3 groups were 7.54$\pm$1.90 mg/dl, 11.78$\pm$6.55 mg/dl and 17.46$\pm$8.69 mg/dl. In this study 31% patients with HbA1c level <7%, 91.8% patients with HbA1c level 7-10%, 81.8% patients with HbA1c level >10% had musculoskeletal deformity. It shows increased prevalence of musculoskeletal deformity/disease with increased levels of HbA1c.In this study 5(17.2%), 35(89.7%) and 32(100%) patients with duration of diabetes <5 years, 5-10 years, >10 years respectively had musculoskeletal deformity. This shows significantly increased prevalence of musculoskeletal disorder with increasing duration of diabetes. (<0.0001) In this study 1st tertile of CRP 17 (51.5%) patients had Musculoskeletal deformity, in 2nd tertile 25 (73.5%) patients had muscular

deformity while in 3rd tertile 30 (90.9%) patients had muscular deformity. It shows increased incidence of musculoskeletal deformity with higher tertile or increased CRP levels. This difference was statistically significant($p<0.0001$).

## Conclusion

This study showed the relationship of inflammation markers, represented by CRP, and glycaemic control represented by HbA1c and duration of diabetes with musculoskeletal disorders. HbA1c increased significantly as CRP and duration of disease increases. These all parameters correlated positively with the musculoskeletal disorders developed as sequela of diabetes. As CRP is an established marker of inflammation and also cardiovascular disease marker, it is important to estimate the CRP and HbA1c levels in diabetics and treat them early to reduce risk of musculoskeletal deformities apart from cardiovascular risk reduction.

## References


1. Smith LL, Burnet SP, McNeil JD. Musculoskeletal manifestations of diabetes mellitus. Br J Sports Med 2003; 37(1): 30–5.
2. Alvin C Power. Diabetes mellitus. In: Kasper DL, Braunwald E, Fauci A, Hauser S, Longo D Jameson JL (eds.). Harrison's Principle of Internal Medicine. 16.ed. McGraw-Hill, 2004; 3779–829.
3. Cagliero E. Rheumatic manifestations of diabetes mellitus. Curr Rheumatol Rep. 2003; 5: 189-94.
4. Ford ES: Body mass index, diabetes, and C-reactive protein among U.S. Adults. Diabetes Care. 1999; 22:1971–1977.
5. Forouzanfar M. H. et al. Global, regional, and national comparative risk assessment of 79 behavioural, environmental and occupational, and metabolic risks or clusters of risks, 1990–2015: a systematic analysis for the Global Burden of Disease Study 2015. Lancet. 2016; 388:1659–1724.
6. Bragg, F. et al. Association between diabetes and cause-specific mortality in rural and urban areas of China. JAMA. 2017; 317: 280–289.
7. Karter A.J., Schillinger D., Adams A.S., Moffet H.H., Liu J., Adler N.E., Kanaya A.M. Elevated rates of diabetes in Pacific Islanders and Asian subgroups: The Diabetes Study of Northern California (DISTANCE) Diabetes Care. 2013; 36:574–579.
8. Smith LL, Burnet SP, McNeil JD. Musculoskeletal manifestations of diabetes mellitus. British Journal of Sports Medicine. 2003; 37:30–35.
9. Khan MI, Weinstock RS. Chapter 16: Carbohydrates. In: McPherson RA, Pincus MR, editors. Henry's Clinical Diagnosis and Management by Laboratory Methods. 22nd ed. Philadelphia, PA: Saunders Elsevier; 2011; 210–25.
10. Shine B, de Beer FC, Pepys MB. Solid phase radioimmunoassay for C-reactive protein. Clin. Chim. Acta. 1981; 117:13–23.
11. Cagliero E. Rheumatic manifestations of diabetes mellitus. Curr Rheumatol Rep. 2003; 5: 189-94.
12. Aydeniz A, Gursoy S, Guney E. Which musculoskeletal manifestation is most seen in type 2 diabetics? J Int Med Res 2008; 36: 505_11.
13. Dana E. King, Arch G. Mainous III, Thomas A. Buchanan, William S. Pearson, Diabetes Care, May 2003; 26(5).
14. A. Majjad, Y. Errahali, H. Toufik, J. H Djossou, M. A. Ghassem, J. Kasouati, and A. E. Maghraoui. Musculoskeletal Disorders in Patients with Diabetes Mellitus: A Cross-Sectional Study International Journal of Rheumatology Volume 2018, Article ID 3839872, 6.
15. Tariq Ahmed Bhat, Shabir Ahmed Dhar, Tahir Ahmed Dar, Muzzaffar Ahmed Naikoo, Mubarik Ahmed Naqqash, Ajaz Bhat, Mohammed

Farooq Butt, The Musculoskeletal Manifestations of Type 2 Diabetes Mellitus in a Kashmiri Population International Journal of Health Sciences, Qassim University, Jan-Mar 2016; 10(1).
16. Córdoba Guzmán, A. C., & castro Daza, E. M. Heyde syndrome as a presentation of acquired Von Willebrand syndrome: what the gastroenterologist should know. Journal of Medical Research and Health Sciences. 2022; 5(7): 2072–2082.