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BRIEF REPORT

# Factors associated with regional rheumatic pain disorders in a population of Puerto Ricans with diabetes mellitus

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**Abstract** The aim of the study was to determine the prevalence and factors associated with bursitis/tendonitis disorders in Puerto Ricans with diabetes mellitus (DM). A cross-sectional study was performed in 202 adult Puerto Ricans (100 DM patients and 102 non-diabetic subjects). For each participant, a complete medical history and a musculoskeletal exam were systematically performed. Socio-demographic parameters, health-related behaviors, comorbidities, and pharmacotherapy were determined for all subjects. For DM patients, disease duration, glycemic control, and DM long-term complications were also examined. Multivariate logistic regression analyses were used to determine the factors associated with bursitis/tendonitis disorders. The mean (SD) age for DM patients and non-diabetic controls were 53.3 (12.9) and 50.0 (13.1) years; 64.0 and 64.7 % of DM patients and controls were females, respectively. Overall, the prevalence of bursitis/tendonitis was higher in DM patients than among non-diabetics (59.0 % vs. 29.4 %, $p<0.01$). In multivariate analyses, DM patients had 2.47 (95 % CI 1.05, 5.84) the odds of having bursitis/tendonitis as compared to non-diabetics. Specifically, DM patients had a higher frequency of flexor tenosynovitis, De Quervain's tenosynovitis, lateral epicondylitis, medial epicondylitis, trochanteric bursitis, and anserine bursitis than non-diabetic subjects ($p<0.05$). Among DM patients, multivariate analyses showed that those with bursitis/tendonitis were more likely to be female [OR (95 % CI) 4.55 (1.42, 14.55)] and have peripheral vascular disease [OR (95 % CI) 8.48 (1.71, 41.93)]. In conclusion, bursitis/tendonitis disorders were common in this population of Hispanics with DM. Among DM patients, bursitis/tendonitis disorders were more frequent in women and those with long-term complications such as peripheral vascular disease.

**Keywords** Bursitis · Diabetes mellitus · Hispanics · Puerto Rico · Regional rheumatic pain disorders · Tendonitis

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## Introduction

Diabetes mellitus (DM) is a chronic metabolic disease associated with a wide variety of complications including renal disease, peripheral neuropathy, retinopathy, and vascular events. Due to its multi-systemic nature, the development of additional manifestations such as musculoskeletal complications is possible [1, 2]. High glucose levels may affect the connective tissue by the formation of advanced glycation end products (AGEs) [3]. In fact, a high prevalence of rheumatic conditions has been previously reported in patients with DM including adhesive capsulitis, Dupuytren's contractures, flexor tenosynovitis, and limited joint mobility [1, 2, 4, 5]. Rheumatic disorders in DM have been associated with disease duration, degree of metabolic control, and the presence of end-

organ damage [6–8]. However, data about the association of DM with specific manifestations such as bursitis and tendonitis syndromes are limited. Moreover, most of these studies have focused in a single regional rheumatic pain disorder and have not included control groups [7–11]. Thus, the aims of this study were to determine the prevalence of regional rheumatic pain disorders in a population of Hispanics with DM patients and non-diabetic subjects and to evaluate their association with socio-demographic parameters, comorbidities, glycemic control, long-term manifestations, and pharmacologic therapy among DM patients.

## Methods

A cross-sectional study was performed in adult DM patients and non-diabetic subjects from Puerto Rico. DM patients were ≥21 years old and fulfilled the National Diabetes Data Group Classification which defines diabetes as present from any two of the following tests on different days: (1) symptoms of diabetes *plus* casual plasma glucose concentration≥200 mg/dL [11.1 mmol/L], (2) fasting plasma glucose≥126 mg/dL [7.0 mmol/L], or (3) 2-h plasma glucose≥ 200 mg/dL [11.1 mmol/L] during an oral glucose tolerance test [12]. All study participants were recruited from the outpatient endocrinology clinics at the University of Puerto Rico Medical Sciences Campus from March 2006 to March 2008. Recruitment of non-diabetic subjects included patients' friends or neighbors accompanying diabetic patients to their scheduled medical visit. Patients' relatives were excluded. An informed consent was obtained for all individuals willing to participate. The study was approved by the Institutional Review Board of the University of Puerto Rico Medical Sciences Campus.

For each patient, a complete medical and musculoskeletal examination was performed in a standard manner by one of the principal investigators (YMF or LECS). Bursitis/tendonitis disorders were ascertained by physical examination as described in the Appendix. In addition, at study visit, a structured questionnaire was completed for each participant to gather data about socio-demographic features, health-related behaviors, and comorbidities.

### Variables

For all study participants socio-demographic parameters, health-related behaviors, and comorbidities were studied. Socio-demographic features included gender, age, level of education, marital status, and annual income. Among health-related behaviors, smoking, alcohol use, exercise, and body mass index (BMI in kilogram per square meter) were evaluated. Comorbidities included rheumatoid arthritis (RA), systemic lupus erythematosus (SLE), hypothyroidism, hyperthyroidism, gout, osteoarthritis (OA), chronic back pain, fibromyalgia, dyslipidemia (hypercholesterolemia and/or hypertriglyceridemia), arterial hypertension, coronary artery disease, obstructive pulmonary disease, depression, anxiety, and malignancy.

For DM patients, disease duration, fasting blood glucose, glycemic control, DM long-term complications, and diabetes treatment (use of insulin and/or oral medication) were also examined. Glycemic control was evaluated using an average of the previous three measurements of glycosylated hemoglobin (HgA1c). DM complications including neurologic complications (peripheral neuropathy, gastroparesis, neurogenic bladder, and cerebrovascular accidents), renal disease (microalbuminuria and end-stage renal disease (ESRD)), retinopathy (non-proliferative and proliferative), cataracts, and cardiovascular complications (peripheral vascular disease, myocardial infarction, angina, percutaneous coronary angioplasty (PTCA), coronary artery bypass graft (CABG), and congestive heart failure) were studied. Finally, the use of insulin and oral DM medications was determined.

### Statistical analysis

Univariate analysis was done using the mean (standard deviation, SD), median (25th and 75th percentiles) for continuous data, and frequencies and percentages for categorical data. Bivariate analysis was done using the unpaired *t* test (or Mann-Whitney *U* test when appropriate) for continuous data and the Pearson chi-square statistics (or Fisher's exact test) for categorical data.

To evaluate the association of DM status with bursitis/tendonitis as well as with socio-demographic characteristics, health-related behaviors, and clinical covariates, contingency tables were constructed. Odds ratios (ORs) and their 95 % confidence intervals (95 % CI) were also calculated. An unconditional multivariate logistic regression analysis was performed to evaluate the association between DM and bursitis/tendonitis after adjustment for covariates with $p<0.10$ in bivariate analysis. The evaluation of interaction terms between bursitis/tendonitis with covariates associated with diabetes was done, and a significant interaction was observed between bursitis/tendonitis and anxiety ($p=0.049$); thus, the final model for the association between diabetes and bursitis/tendonitis for the complete study sample was adjusted to account for the interaction.

A sub-analysis was done among DM patients ($N=100$) to assess the role of study covariates with bursitis/tendonitis using contingency tables, ORs, and 95%CI. Variables with a $p$ value <0.10 in bivariate analysis were included in a multivariate logistic regression model, and adjustment was done by

age at evaluation and DM duration. Statistical significance for all analyses was set at $p<0.05$. The statistical software STATA version 11 (STATA Corp, College Station, TX, USA) was used to perform the analyses.

## Results

A total of 217 subjects were asked to participate in the study; 15 patients declined to participate. The sample consisted of 202 subjects, 100 DM patients and 102 non-diabetic individuals. Table 1 shows the socio-demographic parameters, health-related behaviors, comorbidities, and regional rheumatic pain disorders among diabetic patients and non-diabetic individuals. DM patients had lower level of education and lower income than non-diabetic subjects ($p<0.05$). In addition, DM patients were more likely ($p<0.01$) to have hypothyroidism, osteoarthritis, dyslipidemia, hypertension, coronary artery disease and anxiety disorder, and higher BMI than non-diabetics.

Overall, the prevalence of bursitis/tendonitis was significantly higher among DM patients than non-diabetic subjects (59.0 % vs. 29.4 %, $p<0.01$). Specifically, DM patients were more likely ($p<0.05$) to have flexor tenosynovitis, De Quervain's tenosynovitis, lateral epicondylitis, medial epicondylitis, trochanteric bursitis, and anserine bursitis (Table 1). In the multivariate analysis, after adjusting for age, education level (<12 years), annual income, BMI, hypothyroidism, OA, dyslipidemia, hypertension, coronary artery disease, depression, and anxiety, DM patients had 2.47 (95 % CI 1.05, 5.84) the odds of having bursitis/tendonitis than non-diabetic subjects (data not shown).

Table 2 shows a subanalysis of the association of socio-demographic parameters, health-related behaviors, and comorbidities with bursitis/tendonitis among the 100 DM patients. DM patients with bursitis/tendonitis were more likely to be female than diabetics without bursitis/tendonitis ($p=0.003$). In addition, the prevalence of comorbid conditions such as OA, chronic back pain, and major depression was significantly increased among diabetics with bursitis/tendonitis. A marginal tendency of higher prevalence of hypothyroidism ($p=0.054$) was also observed among diabetics with bursitis/tendonitis.

Glycemic control, DM long-term complications, and treatment modalities of DM patients are depicted in Table 3. Patients with bursitis/tendonitis disorders were more likely to have long-term DM complications such as cataracts and peripheral vascular disease ($p<0.01$). No significant association was found for DM duration, fasting blood glucose, and glycemic control (as measured by mean HgA1c), neurologic involvement, renal involvement, and retinopathy. Both groups were similar in terms of DM pharmacological treatments.

**Table 1** Socio-demographic parameters, health-related behaviors, comorbidities, and regional rheumatic pain disorders among diabetic patients and non-diabetic individuals ($N=202$)

| Feature | DM patients ($n=100$) | Non-diabetics ($n=102$) | $p$ value |
|---|---|---|---|
| Socioeconomic-demographic | | | |
| Gender, % female | 64.0 | 64.7 | 0.917 |
| Age at study visit, mean (SD) years | 53.3 (12.9) | 50.0 (13.1) | 0.069 |
| Education, mean (SD) years | 9.7 (3.9) | 12.2 (4.2) | <0.001 |
| Married, % | 65.0 | 61.4 | 0.595 |
| Income<US$10,000, % | 39.0 | 25.5 | 0.040 |
| Health-related behaviors, % | | | |
| Smoking | 13.0 | 7.8 | 0.256 |
| Alcohol abuse | 1.0 | 3.9 | 0.369 |
| Exercise | 30.0 | 28.4 | 0.806 |
| Body mass index, mean (SD), kg/m$^2$ | 32.3 (7.3) | 28.1 (5.0) | <0.001 |
| Comorbid conditions, % | | | |
| Rheumatoid arthritis | 0.0 | 0.0 | – |
| Systemic lupus erythematosus | 2.0 | 0.0 | 0.244 |
| Hypothyroidism | 22.0 | 2.9 | <0.001 |
| Hyperthyroidism | 4.0 | 3.9 | 0.999 |
| Gouty arthritis | 1.0 | 0.0 | 0.999 |
| Osteoarthritis | 49.0 | 26.5 | 0.001 |
| Chronic back pain | 41.0 | 35.3 | 0.404 |
| Fibromyalgia | 5.0 | 1.0 | 0.117 |
| Dyslipidemia | 62.0 | 18.6 | <0.001 |
| Hypertension | 68.0 | 25.5 | <0.001 |
| Coronary artery disease | 29.0 | 5.9 | <0.001 |
| Obstructive pulmonary disease | 4.0 | 1.0 | 0.167 |
| Major depression | 25.0 | 15.7 | 0.100 |
| Anxiety disorder | 16.0 | 6.9 | 0.041 |
| Malignancy | 8.0 | 5.9 | 0.554 |
| Bursitis/tendonitis (overall), % | 59.0 | 29.4 | <0.001 |
| Flexor tenosynovitis | 17.0 | 3.9 | 0.002 |
| De Quervain's tenosynovitis | 8.0 | 1.0 | 0.018 |
| Lateral epicondylitis | 20.0 | 3.9 | <0.001 |
| Medial epicondylitis | 16.0 | 1.0 | <0.001 |
| Olecranon bursitis | 2.0 | 0.0 | 0.244 |
| Rotator cuff tendonitis | 10.0 | 7.8 | 0.591 |
| Bicipital tendonitis | 9.0 | 2.9 | 0.069 |
| Trochanteric bursitis | 25.0 | 12.8 | 0.026 |
| Pre-patellar bursitis | 3.0 | 0.0 | 0.119 |
| Anserine bursitis | 38.0 | 16.7 | 0.001 |

*DM* diabetes mellitus, *SD* standard deviation

Estimates of the association strength between bursitis/tendonitis and study variables in DM cases are depicted in Table 4. In univariate analyses, increased odds of bursitis/tendonitis were observed among females and in those with

**Table 2** Socio-demographic parameters, health-related behaviors, and selected comorbidities in diabetic patients with and without bursitis/tendinitis (*N*=100)

| Feature | Bursitis/ tendinitis (*n*=59) | No bursitis/ tendinitis (*n*=41) | *p* value |
|---|---|---|---|
| Socio-demographic features | | | |
| Gender, % female | 76.3 | 46.3 | 0.003 |
| Age at evaluation, mean (SD) years | 49.7 (21.1) | 41.3 (25.9) | 0.862 |
| Disease duration, mean (SD) years | 11.6 (10.0) | 10.2 (11.1) | 0.510 |
| Education, mean (SD) years | 9.6 (3.8) | 9.7 (3.9) | 0.861 |
| Married, % | 64.4 | 65.9 | 0.999 |
| Income<$10,000, % | 39.0 | 39.0 | 0.999 |
| Health-related behaviors, % | | | |
| Smoking | 11.9 | 14.6 | 0.766 |
| Alcohol abuse | 0.0 | 2.4 | 0.410 |
| Exercise | 28.8 | 31.7 | 0.756 |
| Type 2 diabetes mellitus, % | 91.5 | 78.0 | 0.056 |
| Body mass index, mean (SD) kg/m$^2$ | 32.7 (7.3) | 31.6 (7.3) | 0.471 |
| Comorbid conditions, % | | | |
| Rheumatoid arthritis | 0.0 | 0.0 | – |
| Systemic lupus erythematosus | 3.4 | 0.0 | 0.511 |
| Hypothyroidism | 28.8 | 12.2 | 0.054 |
| Hyperthyroidism | 1.7 | 7.3 | 0.302 |
| Gouty arthritis | 0.0 | 0.0 | – |
| Osteoarthritis | 62.7 | 29.3 | 0.001 |
| Chronic back pain | 49.2 | 29.3 | 0.047 |
| Fibromyalgia | 8.5 | 0.0 | 0.076 |
| Dyslipidemia | 62.7 | 61.0 | 0.999 |
| Hypertension | 67.8 | 68.3 | 0.999 |
| Obstructive pulmonary disease | 5.1 | 2.4 | 0.642 |
| Major depression | 33.9 | 12.2 | 0.018 |
| Anxiety disorder | 18.6 | 12.2 | 0.423 |
| Malignancy | 11.9 | 2.4 | 0.136 |

*SD* standard deviation

**Table 3** Glycemic control, long-term diabetes complications, and treatment modalities of diabetic patients with and without bursitis/tendonitis (*N*=100)

| Feature (%) | Bursitis/ tendinitis (*n*=59) | No bursitis/ tendinitis (*n*=41) | *p* value |
|---|---|---|---|
| DM duration, mean (SD) years | 11.6 (10.0) | 10.2 (11.1) | 0.510 |
| Fasting blood sugar, mean (SD) mg/dl | 143.5 (71.7) | 171.0 (103.0) | 0.357 |
| Glycosylated Hg, mean (SD) % | 8.3 (2.0) | 8.5 (2.6) | 0.959 |
| Neurologic involvement, % | 54.2 | 46.3 | 0.437 |
| Peripheral neuropathy | 47.5 | 39.0 | 0.403 |
| Gastroparesis | 3.4 | 0.0 | 0.511 |
| Neurogenic bladder | 10.2 | 4.9 | 0.466 |
| Cerebrovascular accident | 6.8 | 7.3 | 0.999 |
| Renal involvement, % | 42.4 | 34.2 | 0.407 |
| Microalbuminuria | 20.3 | 17.1 | 0.682 |
| End-stage renal disease | 3.4 | 2.4 | 0.999 |
| Retinopathy, % | 27.1 | 17.1 | 0.240 |
| Non-proliferative | 11.9 | 9.8 | 0.999 |
| Proliferative | 16.9 | 7.3 | 0.229 |
| Cataracts, % | 27.1 | 4.9 | 0.007 |
| Cardiovascular complications, % | 37.3 | 26.8 | 0.274 |
| Peripheral vascular disease | 27.1 | 4.9 | 0.004 |
| Myocardial infarction | 11.9 | 9.8 | 0.999 |
| Angina | 16.9 | 19.5 | 0.743 |
| PTCA | 3.4 | 0.0 | 0.511 |
| CABG | 5.1 | 0.0 | 0.267 |
| Congestive heart failure | 1.7 | 2.4 | 0.999 |
| DM treatments, % | | | |
| Insulin alone | 23.7 | 26.8 | 0.725 |
| Oral medications alone | 33.9 | 24.4 | 0.308 |
| Oral medications + insulin | 40.7 | 48.8 | 0.422 |

*DM* diabetes mellitus, *SD* standard deviation, *Hg* hemoglobin, *PTCA* percutaneous coronary angioplasty, *CABG* coronary arteries bypass graft

OA, major depression, cataracts, and peripheral vascular disease. In multivariate analyses, only female gender [OR (95 % CI) 4.55 (1.42, 14.55)] and peripheral vascular disease [OR (95 % CI) retained significance.

## Discussion

It is known that diabetic patients are at increased risk of serious complications such as vascular, neurologic, and renal complications. Although a high frequency of musculoskeletal disorders has been reported in DM, their impact is usually being disregarded in the clinical setting. The present study was performed in Hispanics from Puerto Rico, an ethnic group with a high prevalence of DM [13]. We found that diabetic patients were more likely to have bursitis and tendonitis disorders than non-diabetic subjects. Specifically, a higher prevalence of flexor tenosynovitis, De Quervain's tenosynovitis, lateral epicondylitis, medial epicondylitis, trochanteric bursitis, and anserine bursitis was observed in DM patients. In a multivariate analysis among diabetic patients, tendonitis/bursitis was associated with female gender and peripheral vascular disease. No association was found for glycemic control and other DM complications.

In agreement with other studies, we found that regional rheumatic pain disorders are common in patients with DM

**Table 4** Univariate and multivariate models for the presence of bursitis/tendonitis among diabetic patients

| Characteristic | Univariate[a] OR (95 % CI) | Multivariate[b] OR (95 % CI) |
|---|---|---|
| Female gender | 3.72 (1.58–8.79) | 4.55 (1.42–14.55) |
| Type 2 diabetes mellitus | 3.04 (0.93–9.86) | 2.30 (0.37–14.05) |
| Hypothyroidism | 2.91 (0.98–8.69) | 2.03 (0.51–6.49) |
| Osteoarthritis | 4.06 (1.72–9.56) | 2.28 (0.88–8.11) |
| Chronic back pain | 2.34 (1.00–5.44) | 1.22 (0.42–3.59) |
| Major depression | 3.69 (1.25–10.87) | 1.86 (0.49–7.03) |
| Cataracts | 7.26 (2.01–26.26) | 4.08 (0.93–17.90) |
| Peripheral vascular disease | 7.26 (1.57–33.59) | 8.48 (1.71–41.93) |

*OR* odds ratio, *CI* confidence interval

[a] Analysis included variables with $p<0.10$ on the bivariate analysis (Table 3)

[b] Adjusted by age, disease duration, and variables with $p<0.10$ on the bivariate analysis

[14–16]. Higher prevalence of flexor tenosynovitis and anserine bursitis has been reported before for DM patients [15, 16]. In addition, we found De Quervain's tenosynovitis, lateral epicondylitis, medial epicondylitis, and trochanteric bursitis to occur more frequently in DM patients than non-diabetic controls.

In the multivariate analysis, we observed that diabetic patients with bursitis/tendonitis were more likely to be female. This association has been previously reported [16, 17]. Cohen et al. found a strong correlation between non-insulin-dependent DM and anserine bursitis especially among women [16]. In agreement with our study, they did not find an association with age, BMI, and glycemic control. Cagliero et al. also showed a correlation between DM and rheumatic disorders, especially among females and those with long-term DM complications [17].

The association of tendonitis/bursitis with peripheral artery disease in our study is interesting because both disorders may share similar pathophysiologic mechanisms. Advanced glycosylation end products accumulate in proteins of DM patients faster than in non-diabetic subjects [18]; this may lead to tendinopathy as well as to vasculopathy. Also, vascular endothelial growth factor, which is associated with DM vascular disease, appears to be involved in the synovial proliferation of the subacromial bursa and shoulder joint contraction in type 2 DM patients with rotator cuff tendinopathy [19]. Finally, Rosenbloom et al. demonstrated an association between limited joint mobility syndrome and microvascular disease, suggesting that alterations in periarticular connective tissue are related to changes occurring in the microvasculature [20].

Contrary to other works, we did not find an association of bursitis/tendonitis with obesity, glycemic control, and long-term DM complications such as neurologic involvement, nephropathy, and retinopathy. Even though our diabetic patients had a significantly higher BMI as compared to non-diabetic subjects, an association between regional rheumatic pain syndromes and BMI was not observed in the subanalysis among DM patients. At present, the role of obesity in rheumatic disorders is still controversial. Earlier works have found a significant higher prevalence of greater trochanteric syndrome among obese subjects although the association was not sustained in multivariate analysis [21]. Among other negative results, our study failed to find and association between bursitis/tendonitis and glycemic control. Nonetheless, glycemic control is an important factor to be considered to reduce not only the burden of micro- and macrovascular complications of diabetes [22], but perhaps the occurrence of rheumatic complications as other studies have linked musculoskeletal disorders with long-term glycemic control [23].

This study has some limitations. First, because this work was a cross-sectional study, we could not ascertain if study subjects had prior episodes of bursitis and/or tendinitis. Second, this study was performed in Puerto Ricans evaluated in a university-based center in San Juan, Puerto Rico; thus, the results are not intended to be generalized to the entire population of Puerto Rico or to other ethnic groups. Third, DM status of non-diabetic subjects was self-reported; therefore, the possibility of misclassification bias must be acknowledged; however, the effect of the misclassification would be to underestimate the association of DM and rheumatic pain syndromes, not to overestimate it. Finally, the diagnosis of regional rheumatic pain disorders was based solely on clinical examination and not on imaging studies such as ultrasonography or magnetic resonance. For instance, patients with low back pain and fibromyalgia syndrome may have regional pain and tenderness without having underlying tendinitis/bursitis.

Despite these limitations, the present study has some clinical implications. We found that Puerto Ricans with DM are commonly affected by bursitis and tendonitis disorders, particularly women and those with long-term complications such as peripheral artery disease. Physicians are mainly concerned about cardiovascular, renal, and ocular complications in DM patients because of their impact on the morbidity and mortality. However, our study shows that regional rheumatic pain disorders, which may pose a considerable impairment to their quality of life, are highly prevalent in this population, and therefore, they should not be overlooked by primary care physicians.

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**Disclosures** None.

## Appendix

**Table 5** Regional rheumatic pain disorders examined

| Rheumatic pain disorder | Definition |
|---|---|
| Dupuytren's contracture | Presence of palpable thickening of palmar fascia and flexor deformity of the second, third, fourth, and fifth fingers |
| Flexor tenosynovitis | Palpable nodule or thickening flexor tendon, and/or locking during extension and flexion of any finger |
| De Quervain's tenosynovitis | Pain and tenderness over radial styloid with a positive Finkelstein maneuver |
| Olecranon bursitis | Pain, tenderness, and swelling at the location of the olecranon bursa |
| Lateral epicondilytis | Pain and tenderness over the medial epicondyle with pain against resistance on wrist extension |
| Medial epicondilytis | Pain and tenderness over the medial epicondyle with pain against resistance on wrist flexion |
| Rotator's cuff tendinitis | Shoulder pain on active abduction (specially 60° and 120°), tenderness over the greater tuberosity, and positive impingement sign |
| Bicipital tendinitis | Anterior shoulder pain worsened with active flexion, tenderness over the bicipital groove, and positive Yergason's maneuver and/or Speed's test |
| Trochanteric bursitis | Pain and tenderness at the location of the trochanteric bursa |
| Pre-patellar bursitis | Pain, tenderness, and swelling at the location of the pre-patellar bursa |
| Anserine bursitis | Pain, tenderness, and swelling at the location of the anserine bursa |

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