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Research

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Clinical Factors Associated with Musculoskeletal Injuries in Children and Adolescents with Diabetes Mellitus

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Abstract

Background: To examine the incidence of traumatic and overuse Musculoskeletal Injuries (MSI) in children and adolescents with diagnosed diabetes mellitus, which has been understudied.

Methods: Using a population-based, retrospective cohort design and South Carolina's (USA) Medicaid claims dataset covering outpatient and inpatient medical services, and medication prescriptions over an 11-year period for patients ≤ 17 years of age with ≥ 2 visits for ICD-9 diagnostic codes for diabetes mellitus, a cohort of 5448 cases was identified and analyzed using logistic regression to compare risk factors for those who sustained MSIs with those who did not.

Results: Incident joint, back, or muscle pain, contracture, spasms, or swelling were diagnosed, in addition to upper limb fractures and sprains, costochondritis, and stress fractures, usually in adolescence. Comorbid obesity (30.6%), dyslipidemia (22.9%), primary hypertension (18.7%), substance use disorder (7.4%), and arrhythmia (5.6%) were diagnosed in the cohort as were peripheral neuropathy (2.7%) and early cardiovascular disease (5.5%). While traumatic fractures and concussions were more closely associated with cardiovascular conditions and substance abuse, sprains, dislocations, and all micro-traumatic, overuse injuries were associated with comorbid obesity, dyslipidemia, and hypertension, as well as with less-frequent incident arrhythmia, and the cardiovascular and peripheral neuropathy complications of diabetes.

Conclusions: These findings add to the existing, primarily adult, literature regarding the musculoskeletal manifestations of diabetes and cardio-metabolic disorders in youth and update the knowledge base of pediatric practitioners to enable them to better anticipate the clinical care needs of such patients and provide them more effective care.

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Introduction

Over recent decades, a decline in the daily physical activity level of children and adolescents has been noted, with a concomitant "explosion" in the number of children diagnosed at an early age with obesity, hypertension, dyslipidemia, and Diabetes Mellitus (DM), leading to a higher prevalence of comorbid chronic medical conditions, and incident traumatic or micro-traumatic, overuse Musculoskeletal Injuries (MSI) in youth [1-4]. Children with DM have been shown to be at a higher risk for lipid abnormalities, hypertension, and overweight/obesity, but are less likely to receive recommended screening and treatment than nondiabetic children [5, 6]. Recognizing the long-term, detrimental influence of the vascular complications of DM in growing children, we will focus on DM as the core disease in this analysis, while recognizing the substantial role of comorbid obesity, hypertension, and dyslipidemia as independent risk factors for the development of cardiovascular disease, peripheral neuropathy, and other DM complications regardless of age or type of DM [5, 6].

Previous studies of DM in adults have identified limited joint mobility, stiff hand syndrome, diabetic muscular infarction, Dupuytren's disease, shoulder capsulitis, neuropathic arthropathy

and neuropathy, flexor tenosynovitis, and carpal tunnel syndrome as its predominant musculoskeletal manifestations [7-10]. However, the musculoskeletal manifestations of DM and its related cardio-metabolic disorders in children remain understudied or unreported [6]. In this epidemiologic investigation, we examine the incidence of Musculoskeletal Injuries (MSI) evident over time in a large, heterogeneous cohort of youth with DM and related cardio-metabolic disorders, controlling for DM disease severity (i.e., number and type of complications), insulin treatment, and the presence of each comorbid cardio-metabolic disorder.

Methods

Study Population and Data

Medical and pharmacy claims for the calendar years January 1, 1996 through December 31, 2006 were used to identify a cohort of children and adolescent patients (ages 17 and under) enrolled in and eligible for Medicaid for a minimum of 9 months in each calendar year included in this analysis, who had a service encounter with a diagnosis of Type 1, Type 2, or diabetes unspecified (250.xx) using ICD-9 diagnostic codes (International Classification of Disease 9th Clinical Modification). In this pediatric population, we have previously found that the two types of diabetes are sometimes misclassified or not specified, leading to similar patterns of complications, e.g., neuropathy, diabetic ketoacidosis, etc [11]. Furthermore, previous studies have found the patterns of musculoskeletal manifestations of DM to be very similar between the two types [7, 8]. Therefore, we have selected a broadly-defined DM cohort to investigate. Age at DM diagnosis was the first visit in which the DM diagnosis was documented in the Medicaid claims files.

Primary or secondary diagnosis codes for nine categories of MSI were coded: fracture (800-829), dislocation (830-839), sprain (840-848), concussion (850-854), thorax/abdomen/ pelvis (860-869), arthropathies/connective tissue disorders (710-719); dorsospinal disorders (720-724), muscle/joint disorders (725-729), and bone/cartilage disorders (730-739). The following categories of comorbid cardio-metabolic disorders were also coded: obesity (278; 278.00; 278.01), dyslipidemia (272.0-272.9), and essential hypertension (401.x). As in most epidemiologic studies employing existing administrative data sets, we did not have access to HbA1c values over time as the primary marker of glycemic control. We assumed, based on studies by previous investigators [5, 6], that the risk of developing diabetes-related comorbid health conditions is negatively correlated with HbA1c, so we emphasized treatment with insulin and the development of neuropathy and cardiovascular complications to indicate the progression of the DM. Complications arising from DM which has progressed due to insufficient HbA1c control were coded as: cardiovascular disease (410.0-414.9; 415.0-417.9; 420.0-429.9), arrhythmia (427.x), and peripheral neuropathy (337xx, 250.6). Finally, a comorbid substance use disorder (304.x or 305.x) was coded because of the increasing prevalence of substance use among adolescents and its deleterious effects. All cases with diagnosed congenital heart disease or genetic syndromes were excluded. The prescription of insulin was also coded as the number of months an insulin prescription was filled/refilled from the Medicaid Pharmacy file. This study was approved by the University of South Carolina Institutional Review Board as exempt from human subject research guidelines due to the use of existing and de-identified clinical data sets.

Statistical Analyses

Descriptive statistical analyses were performed to determine the prevalence of each injury category and any bivariate associations between the predictor variables of interest. Because MS injuries result from a complex interaction of multiple risk factors, a multivariate statistical analysis approach was used [12]. Separate multiple logistic regression equations were constructed to assess the relative odds associated with having each of the diagnosed MSI categories, using individual risk factors (age, sex, ethnicity), diagnosed neuropathy or cardiovascular disorders, comorbid metabolic conditions or substance use, and months prescribed insulin as predictor variables. Each fullregression model was then reduced through a stepwise procedure to reflect only the statistically significant variables associated with being diagnosed with each MSI category, using a preset significance level of $p \leq 0.05$. The measure of association reported for these results is the adjusted Odds Ratio (aOR) with a corresponding 95% confidence interval. All statistical analyses were performed in SAS software, version 9.3 (SAS Institute, Cary, North Carolina).

Results

Data from 5448 individuals were analyzed and are characterized in Table 1 as primarily female, and African American (both 56%). The mean age of first DM diagnosis under

Medicaid was 10.1 years, but many were diagnosed in the pre-school years. Insulin was prescribed for 24% of these youth, for a mean of 17.6 months; however, there was considerable variability in the months exposed to insulin. Comorbid cardio-metabolic andother diseases prevalent in the DM cohort were: obesity (30.6%), dyslipidemia (22.9%), primary hypertension (18.7%), substance use disorder (7.4%), and arrhythmia (5.6%). DM complications of neuropathy (2.7%) and early cardiovascular disease (5.5%) were also evident in these youth.

Table 1: Descriptive Characteristics of 5448 Youth Diagnosed With Diabetes Mellitus

Indicator	N (%)
Gender: Female	3039 (55.8)
Male	2409 (44.2)
Race: African American	3032 (55.6)
White	2004 (36.8)
Other	413 (7.6)
Mean Age at First DM Diagnosis (SD)	10.1 (5.3)
Mean Years in Medicaid Dataset (SD)	6.1 (3.0)
Comorbid Medical Conditions	
Diagnosed with Obesity	1665 (30.6)
Diagnosed with Dyslipidemia	1245 (22.9)
Diagnosed with Hypertension	1017 (18.7)
Diagnosed with Substance Use Disorder	405 (7.4)
Musculoskeletal Injuries	
Diagnosed with Fracture	972 (17.8)
Diagnosed with Sprain	1681 (30.9)
Diagnosed with Concussion	184 (3.4)
Diagnosed with Dislocation	186 (3.4)
Diagnosed with Thoracic/Pelvis Injury	52 (0.9)
Diagnosed with Arthropathies/Connective Tissue Disorders	1812 (33.3)
Diagnosed with Dorso/Spinal Disorders	1233 (22.6)
Diagnosed with Muscle/Joint Disorders	1779 (32.7)
Diagnosed with Bone/Cartilage Disorders	827 (15.2)
DM Complications	
Neuropathy	149 (2.7)
Diagnosed with Arrhythmia (supraventricular tachycardia)	303 (5.6)
Diagnosed with Cardiovascular Disease	300 (5.5)
Medication Exposure	
Insulin Exposure	1310 (24.0)
Mean Number of Months of Insulin Exposure (SD)	17.6 (18.1)

Traumatic and Overuse MSI

All of the traumatic or overuse MSIs were diagnosed in late childhood or adolescence. Diagnosed traumatic fractures were most frequent in the upper body, primarily the radius/ulna and hand. Diagnosed sprains were most frequently in the ankle, back, wrist/hand. A vast majority of the joint/connective tissue, dorsal/spinal, and muscle/joint injuries involved joint, back, or muscle pain, contracture, or swelling. However, other noteworthy MSIs were: carpal tunnel syndrome (0.6%), osteoarthritis (1.1%), capsulitis/tendonitis (shoulder and NOS) (3.0%), synovitis/tenosynovitis (4.0%), and muscle spasms (2.2%). Bone and cartilage disorders were also diagnosed in these youth, rimarily costochondritis and stress fractures.

Factors Associated with Incident MSI

As shown in Table 2, several predictor variables were significantly associated with the increased odds of a child or adolescent being diagnosed with more than one of the traumatic MSI categories. The risk of sustaining a fracture was significantly increased having a diagnosed arrhythmia (adjusted Odds Ratio [aOR] =1.83), obesity (aOR=1.27), and substance use disorder (aOR=1.31). The risk of sustaining a sprain was significantly related to being diagnosed with obesity (aOR=1.59), cardiovascular disorder (aOR=1.48), hypertension (aOR=1.21), and a substance use disorder (aOR=1.72). The risk of sustaining a concussion was significantly associated to having a diagnosed cardiovascular disorder (aOR=2.45) or substance use disorder (aOR=1.89). The risk of sustaining a dislocation injury was increased by comorbid obesity (aOR=1.56) and incident neuropathy (aOR=2.45).

Table 2: Adjusted Odds Ratios for Having Eight Types of Musculoskeletal Injuries Related to Comorbid Cardio-Metabolic Conditions, Diabetes Complications, or Individual Risk Factors

Parameter	Adjusted Odds Ratio	95% Confidence Intervals
Fracture		
African American	0.51**	0.44-0.59
Male	1.85**	1.60-2.13
Obesity Diagnosis	1.27*	1.09-1.48
Substance Abuse Diagnosis	1.31*	1.02-1.68
Arrhythmia Diagnosis	1.83**	1.40-2.38
Sprain		
African American	0.76**	0.67-0.86
Obesity Diagnosis	1.59**	1.40-1.82
Substance Abuse Diagnosis	1.72**	1.39-2.14
Hypertension Diagnosis	1.21*	1.03-1.41
Cardiovascular Diagnosis	1.48*	1.15-1.91
Concussion		
African American	0.56*	0.42-0.76
Male	1.82**	1.35-2.47
Substance Abuse Diagnosis	1.89*	1.21-2.94
Cardiovascular Diagnosis	2.45*	1.53-3.91
Dislocation		
African American	0.66*	0.49-0.89
Obesity Diagnosis	1.56*	1.16-2.11
Neuropathy Diagnosis	2.07*	1.07-4.01
Arthropathies/Connective Tissue Disorders		
African American	0.66**	0.59-0.75
Obesity Diagnosis	1.53**	1.35-1.74

Dyslipidemia Diagnosis	1.26*	1.10-1.45
Hypertension Diagnosis	1.26*	1.09-1.47
Cardiovascular Diagnosis	1.96**	1.54-2.50
Neuropathy Diagnosis	1.49*	1.06-2.09
Dorso/Spinal Disorders		
African American	0.62**	0.54-0.72
Female	1.43**	1.24-1.65
Obesity Diagnosis	1.56**	1.36-1.80
Dyslipidemia Diagnosis	1.23*	1.06-1.44
Cardiovascular Diagnosis	1.45*	1.10-1.90
Neuropathy Diagnosis	1.69*	1.18-2.41
Arrhythmia Diagnosis	1.44*	1.10-1.89
Substance Use Disorder	1.73**	1.38-2.16
Muscle/Joint Disorders		
African American	0.82*	0.72-0.92
Obesity Diagnosis	1.61**	1.42-1.83
Dyslipidemia Diagnosis	1.26*	1.10-1.45
Hypertension Diagnosis	1.20*	1.03-1.39
Cardiovascular Diagnosis	1.95**	1.52-2.50
Arrhythmia Diagnosis	1.83**	1.44-2.34
Substance Use Disorder	1.48*	1.19-1.84
Bone/Cartilage Disorders		
Obesity Diagnosis	1.74**	1.48-2.04
Hypertension Diagnosis	1.28*	1.06-1.54
Dyslipidemia Diagnosis	1.29*	1.09-1.53
Cardiovascular Diagnosis	1.86**	1.41-2.45
Arrhythmia Diagnosis	1.55*	1.17-2.07

* Significant at p=.01 or less; ** Significant at p <.0001

For the micro-traumatic, overuse injuries, an increased risk of incident arthropathies/ connective tissue disorders, dorso/spinal disorders, muscle/joint disorders, and bone/cartilage disorders was associated with comorbid diagnoses of obesity (aOR=1.53, 1.56, 1.61, 1.74, respectively), dyslipidemia (aOR=1.26, 1.23, 1.26, 1.29), and incident cardiovascular disorder (aOR=1.96; 1.45, 1.95, 1.86). An increased risk of incident arthropathies/connective tissue disorders, muscle/joint disorders, and bone/cartilage disorders was also associated with comorbid hypertension (aOR=1.26, 1.17, 1.28), whereas an increased risk of incident arthropathies/ connective tissue disorders and dorso/spinal disorders was associated with diagnosed neuropathy (aOR=1.49, 1.69). An increased risk of incident dorso/spinal disorders, muscle/joint disorders, and bone/cartilage disorders was associated with diagnosed arrhythmia (aOR=1.44, 1.83, 1.55). An increased risk of incident dorso/spinal disorders and muscle/joint disorders was associated with diagnosed substance use disorder (aOR=1.65, 1.37).

Discussion

Although the long-term diabetes-related vascular and macrovascular complications should be rare in childhood and adolescence, our findings provide additional documentation that early abnormalities are present in some children within a few years of an initial DM diagnosis, including musculoskeletal manifestations and cardiovascular complications [5, 6]. Macrovascular disease, as evidenced by pain, paresthesia, muscle

weakness, and neuropathy, as well as microvascular cardiac disease and peripheral vascular disease were apparent in this youthful cohort by adolescence. Our findings are generally consistent with the few studies previously conducted among adolescents, and may reflect the less intensive emphasis on screening for DM and its associated cardio-metabolic disorders, and glycemic control among children and adolescents during the time period investigated [6].

Moreover, the cardio-metabolic conditions associated with core DM also play a critical role in disease outcome. Risk factors for the development of diabetes-related complications include older age/adolescence (puberty), hypertension, dyslipidemia, higher BMI/obesity, and being male [5]. Our findings indicate that these risk factors for developing DM complications are also related to incident MSI in youth with DM. The major factors predicting development of a range of incident MSIs in this cohort were the more prevalent comorbid obesity and dyslipidemia disorders, as well as the less frequent arrhythmia, and cardiovascular/peripheral neuropathy complications of DM. Most importantly, there appears to be a core group of adolescents whose presentation may be complicated by multiple comorbid cardio-metabolic conditions and early- onset diabetes complications. Not only are all of the Odds Ratios in Table 2 concerning the significant predictors of MSIs very similar (ranging from 1.xx-2.xx generally), which means these factors were contributing to a similar degree to the MSI examined, but there also were no outlying diagnoses attributable primarily to any one comorbid condition such as obesity, e.g., slipped upper femoral epiphysis, so it is unlikely that any one of the comorbid conditions is more significantly associated with each MSI than the others. To our knowledge, this is the first population-based, epidemiologic study demonstrating the early incidence and confluence of these risk factors as related to MSI outcomes in youth with DM.

Compared to reports concerning diabetes-related musculoskeletal manifestations in adults, predominantly osteoporosis and increased fracture risk, upper limb musculoskeletal abnormalities (shoulder and hand), limited joint mobility, septic arthritis, carpal tunnel syndrome, trigger finger, and Dupuytren's contracture [7-10, 13], we found a range of joint, back, or muscle pain, contracture, spasm, or swelling in these youth, in addition to a preponderance of upper limb fractures and sprains. Other non-traumatic MSIs present were: capsulitis/tendonitis (shoulder and NOS) (3.0%), synovitis/ tenosynovitis (4.0%), osteoarthritis (1.1%), carpal tunnel syndrome (0.6%), infective arthritis (0.2%), but no diagnosed Dupuytren's contracture. These MSIs were present at lower rates than those documented for diabetic adults [7-10, 13].

Recent consensus statements from the American Medical Association and other professional associations have emphasized increased awareness and management of athletes with special medical conditions, such as DM, by team physicians and primary care physicians because exercise is beneficial for these individuals, but to our knowledge there have been no epidemiologic studies of the MSI typically apparent in children and adolescents with DM [4, 14]. Our findings address this knowledge and practice gap. Many youths engaging in routine physical education or recreational sport activities may not be screened or monitored for diabetes and other cardiovascular risk factors (tobacco use, alcohol or stimulant drug abuse, hypertension, and dyslipidemia), end organ damage, as closely as athletes in training or the medical information available to a primary care physician may not be conveyed to school athletic program authorities/health care staff. Early detection and management of these complicated cases represents an ongoing clinical issue and may require involvement by multiple healthcare providers. Furthermore, more intensive medical treatment may be delayed due to misclassification of the diabetes [11] or because children and adolescents with comorbid hypertension or dyslipidemia may appear asymptomatic or the medications are thought to incur additional, unwanted side effects. However, primary care practitioners should note the possible non-cardiovascular, MSI outcomes related to this decision.

While this DM cohort represents a large, heterogeneous group of children and adolescents being treated for diagnosed DM and its associated cardio-metabolic disorders, varying periods of exposure to insulin, and a long-term observational study period regarding incident MSI and the development of DM complications, the data were not gathered using a prospective, controlled methods. Previous studies have found that although observational (Medicaid) databases provide much less detailed information on individuals than primary data collection, the physician diagnoses coded and the utilization data correspond to clinical medical record reviews in the majority of cases [15, 16].

The DM cohort is representative of pediatric patients in routine care settings in the southeastern USA states and other small states as well as some inner cities with predominantly African American communities, but our results may also be generalizable to countries with predominantly small-city and rural populations in terms of age, sex, increasingly diverse racial demographics, and public funding for healthcare [17-19].

Moreover, these results need to be interpreted with several limitations in mind. No structured clinical interviews were employed to confirm any of the diagnoses assigned by the pediatrician/primary care physician or their designation of each diagnosis in the Medicaid billing system. Consequently, the incidence of these conditions (especially concussions) may be an underestimate, which we cannot quantify. As noted previously, data regarding HbA1c values and glycemic control over time or key risk factors such as family history of obesity or related cardio-metabolic disorders were not available to the investigators and are not modeled in these analyses. Moreover, we could not reliably distinguish Type 1 and Type 2 DM based on the physician coding. Children and adolescents who dropped out of treatment or who were periodically ineligible for Medicaid are not represented in this data set. These results report *associations* and, as a result, *directions of causality cannot be inferred*. Finally, although many significant covariates have been controlled for, other unmeasured differences in patients or their treatment, including non-pharmacological treatments, may explain the findings.

In conclusion, our findings demonstrate several quantitative ways in which the prevalence of MSI among complicated cases of early-onset DM in children differ from those noted in the existing literature on diabetic adults, and update the knowledge base of pediatric practitioners to anticipate the clinical care needs of young patients with diabetes and its associated cardio-metabolic disorders, in order to provide them more effective care. Future studies of children and adolescents with DM during the current era in which intensive glycemic control has become the standard of care should indicate the extent to which this standard of care is actually being implemented in a range of clinical settings.

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