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Brief Musculoskeletal Screen and Patient Education for Down Syndrome-Associated Arthritis

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Introduction

Down syndrome (DS) is one of the most common birth defects in the United States with resulting in an estimated birth prevalence of 12.6 per 10 000 live births.[1] DS is characterized by a heterogenous phenotype that results from a dosage imbalance of genes on human chromosome 21.[2] Due to the heterogenous phenotype, broad presentation of presenting symptoms, and complex needs of the child with DS, the American Academy of Pediatrics (AAP) published a clinical report for the health supervision of children with DS.[3] The report discusses age-appropriate guidance on when to screen for specific conditions, when to refer to specialty care for evaluation, and anticipatory guidance for families as their child with DS ages.

Inflammatory arthritis in children with DS was first described in 1984 and was termed Down syndrome arthropathy,[4] however, the term Down syndrome-associated arthritis (DA) has been recommended to better describe the inflammatory nature of the disease.[5] Studies have shown that DA is under-recognized with a delay in diagnosis.[6] Most patients present with polyarticular (5 or more joints with arthritis), rheumatoid factor (RF), and anti-nuclear antibody (ANA) negative disease.[6] There are reports that DA is more prevalent than juvenile idiopathic arthritis (JIA),[5,7] which is the most common pediatric rheumatologic disease.[8] Additionally, DA appears more aggressive than JIA with more bone and joint damage at presentation, and despite aggressive therapy with disease modifying antirheumatic drugs (DMARDs) and biologic therapy, disease burden is higher for those with DA compared to JIA.[9] Despite this the American Academy of Pediatrics does not mention arthritis or screening for arthritis in the clinical report for health supervision of children with DS.

In a national survey of Down syndrome clinic providers, 77% responded that they were aware of the risk for inflammatory arthritis in DS, however, less than half educated families about the risk, which is likely due to the lack of guidance around screening and evaluation for DA.[10] The uncertainty and lack of guidance in screening for DA is a gap in the medial literature. Our objective was to develop and pilot a brief musculoskeletal screen for DA and our secondary objective was to provide education to families about DA.

Methods and Materials

As part of a cross-sectional study, a convenience sample of 91 children with Down syndrome were recruited at routine clinical care visits at 1 tertiary care center, in sequential order over a 6-month period, provided eligibility criteria were met. Patients were eligible if they were between the age of 1 to 17 years of age, and confirmed Down syndrome, and seen in the Down Syndrome Clinic. To confirm diagnosis karyotypes were reviewed, but not collected for report as phenotype is similar despite differences in karyotype.[11] Patients and families were asked 2 brief musculoskeletal screening questions. (1) "Over the past 3 months, have you noticed any joint swelling in your child?" and (2) "Over the past 3 months, have you noticed any morning stiffness in your child?" These questions were chosen specifically to be brief, but also because reports suggest that >75% of patients reported morning stiffness and joint swelling at diagnosis of arthritis.[6,7] If the screening questionnaire was positive (affirmative answer for 1 or both questions), the medical care provider would contact a pediatric

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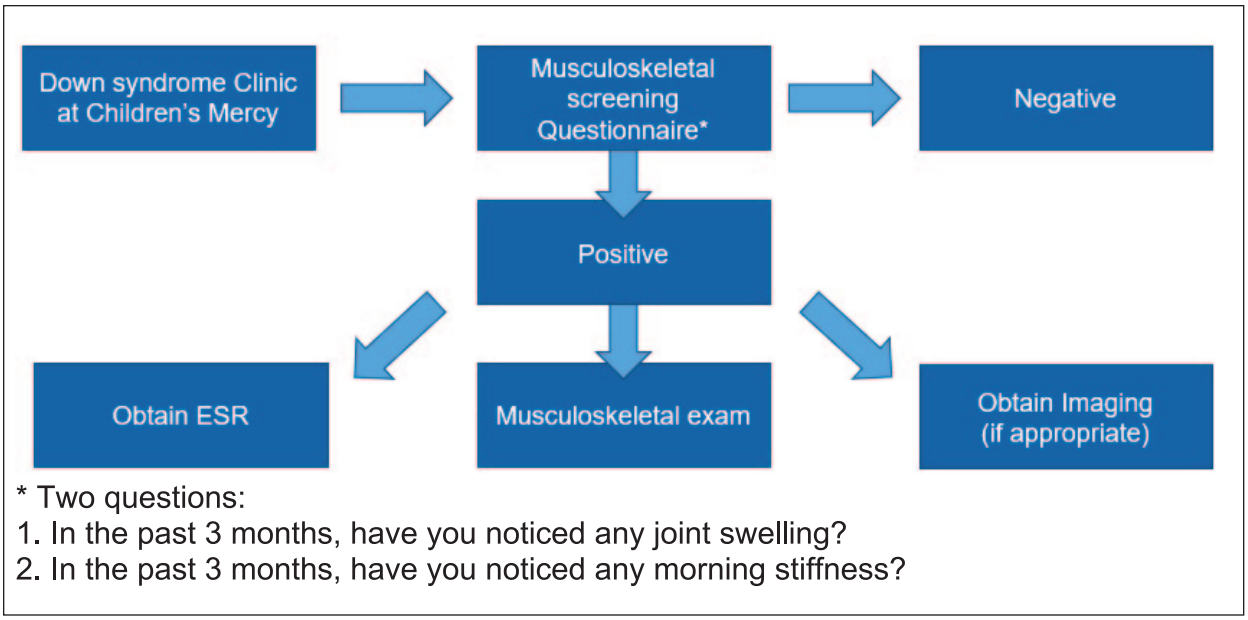

Figure 1. Brief musculoskeletal screen flow diagram.

rheumatology co-investigator to complete a musculoskeletal joint exam to determine if arthritis was present. Additionally, all positive screens had an erythrocyte sedimentation rate (ESR) obtained at the visit as previous studies suggest an elevated ESR is present in the majority of those with DA.[6,7] Imaging studies were obtained if warranted by the pediatric rheumatologist conducting the musculoskeletal exam (Figure 1). If arthritis was present the patient would be treated with standard of care for pediatric inflammatory arthritis. If arthritis was not present, follow-up, if necessary, was determined by the pediatric rheumatologist.

Upon discharge from the DS clinic visit, evidence-based education about DA was provided to all families. A smart form was created to guide medical providers through the education and document completion. This included statements about increased risk of arthritis in children with DS, and signs and symptoms of arthritis (Figure 2). About 1 week after the study visit families completed a phone interview to assess the education and brief musculoskeletal screening at their visit to determine feasibility and implementation in the future. The follow-up questionnaire had multiple choice questions and a place for respondents to fill-in any additional responses or comments. Some questions were asked on a 5-point Likert scale. Gender, age, and ethnicity were collected as demographic information.

The results were analyzed by descriptive statistics and performed using IBM SPSS Statistics version 24.

Ethical Approval and Informed Consent

Written informed consent was obtained from all legal guardians and there was a waiver of assent for the patients. This work was conducted in accordance with the Declaration of Helsinki. Institutional review board approval was obtained from Children's Mercy Kansas City (IRB ID: 16060435).

Results

Of the 91 patients with Down syndrome who were screened, 48 (53%) were male with a mean age of 7.2 years (SD 5.0). Most were Caucasian (77%) followed by African American (11%), and Hispanic (9%). There were 4 positive screens (4%), all (100%) had a normal ESR, and all had imaging studies completed. About 2 had x-rays, which were normal, and 2 had ultrasounds, 1 of which was normal and 1 that was abnormal and consistent with arthritis.

All 91 completed the follow-up questionnaire with 100% (91/91) saying they were comfortable with their child being screened for arthritis in clinic. When asked how they would rate the ease of the screening on a 5-point Likert scale (Extremely easy to Very difficult), 60% (54/91) rated it extremely easy while 40% (37/91) rated it very easy. All 91 reported the musculoskeletal screen was an appropriate use of clinic time at their clinical visit, and they would like their child's primary

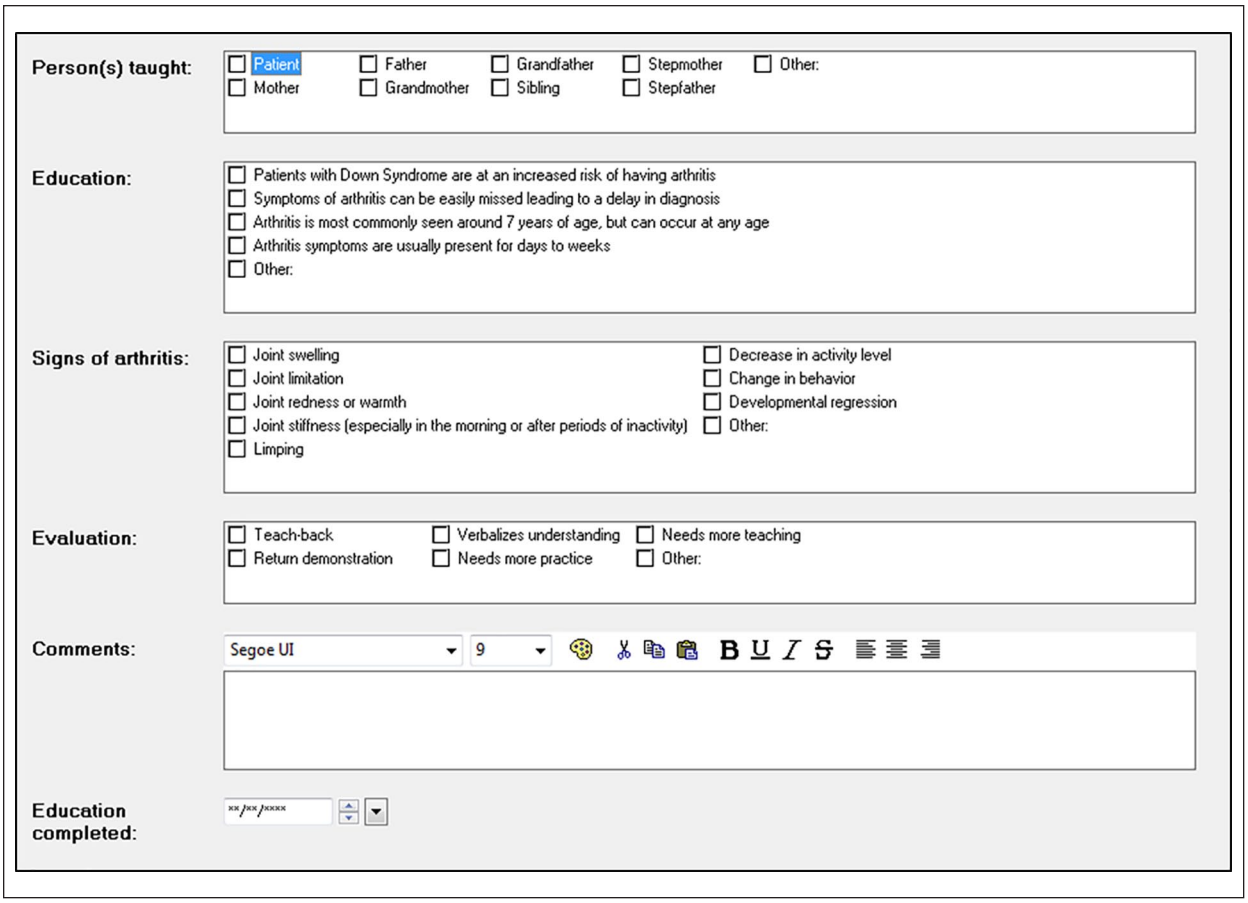

Figure 2. Brief educational information smart form about inflammatory arthritis in Down syndrome that was given to families. This form is fully completed by medical staff to document education and discussion of arthritis with the family.

provider to continue to screen for arthritis at future clinical visits. When parents were asked if they knew their child was at increased risk to develop inflammatory arthritis, 86% (78/91) reported they were unaware of the risk prior to their clinic appointment.

Discussion

Down syndrome-associated arthritis (DA) is a significant cause of musculoskeletal morbidity in children with Down syndrome (DS), and despite the increased risk of DA in patients with DS there is lack of awareness and no formal guidance on screening or surveillance of DA. In the most recent version of the AAP Health Supervision of Children with Down Syndrome,[3] there is no mention of screening or surveillance for arthritis. Other challenges for children with DS are the risk for developmental delays, high pain tolerance, compromised communication skills and noninflammatory musculoskeletal conditions such as ligament laxity and pes planus,[12,13] which may mislead providers and delay diagnosis. As there is no guidance or recommendations for screening for DA, we developed and piloted a brief musculoskeletal screen and provided education that was feasible for families.

Our brief musculoskeletal screen identified 4 patients with musculoskeletal symptoms concerning for inflammatory arthritis, with 1 was ultimately diagnosed with DA, which gives an incidence of 1% for this study. The current prevalence of DA has been reported at 1% to 2%,[5,7] which is like other conditions associated with DS such as atlantoaxial instability, leukemia, and Hirschsprung disease, all of which are mentioned in the clinical report for health supervision of children with DS. The exemption of DA from the health supervision and anticipatory guidance education for children with DS is a contributor to the delay in diagnosis of DA,[6] and likely why the parents in this study are mostly unaware of the risk for inflammatory arthritis in their child. We propose providing education and anticipatory guidance to families about the risk of DA to increase awareness. The parents surveyed did report interest in regular

screening for DA, and the increased awareness may lead to earlier screening, diagnosis, and treatment, which could prevent worse outcomes.

As part of the brief musculoskeletal screen, all positive screens had an ESR obtained to evaluate for systemic inflammation. This was chosen because earlier reports of DA show that many with DA (56%-100%) had an elevated ESR at diagnosis of arthritis,[6,7,14] however, none of the patients in this study had an abnormal ESR. This is more consistent with a recent report that shows that at diagnosis of DA almost half (44%) have normal laboratory tests (CBC, CRP, ESR, RF, ANA), and only 17% had an abnormal CRP and ESR.[9] The difference between the studies is attributed to earlier diagnosis and increased awareness that is supported by a shorter average time to diagnosis of DA (8.3 months) compared to older studies that report a 19-month average time to diagnosis. This indicates that laboratory tests may be less helpful in a screening tool for evaluation of DA.

All positive screens in this study did have imaging obtained. This is likely due to a recent study that showed that children with DA have more radiographic changes consistent with arthritis at diagnosis compared to those with JIA (38% vs 22%).[9] However, with imaging there is a discrepancy in utilization of imaging modalities in screening for DA as imaging is not frequently utilized by Down Syndrome Clinic providers in their evaluation for DA.[10] While the reason for this is unclear, it may be due to limiting radiation exposure in individuals with higher prevalence of malignancy.[15] In comparison, x-rays are the most used imaging modality for pediatric rheumatologists to aid in evaluation of DA,[16] which is likely due to their accessibility and reproducibility. However, x-rays are not sensitive enough to reveal subtle or early arthritis, and ultrasound, which is the second most used imaging modality of pediatric rheumatologist in evaluating DA,[16] has the capabilities to pick up more subtle disease and tendon changes. Ultrasound does have limitations, which includes that it is operator dependent and may not be as reproducible from 1 technician to another[17] or as readily available depending on clinical setting.

Our study has several limitations, which includes the limited number of questions on the musculoskeletal screen, which should be broadened to improve sensitivity, however, we wanted the questions to be focused and brief so to be minimally invasive to clinic flow and easy to administer. We also understand that having a pediatric rheumatologist perform a physical exam for a positive musculoskeletal screen is not feasible at all institutions and a standardized approach for musculoskeletal exam specific for those with DS that could be easily administered by primary care providers should be developed for DA. Another limitation was the imaging discretion for joints that were suspicious for arthritis by the pediatric rheumatologist, which was inconsistent as x-rays and ultrasound were used instead of clear guidance on imaging approach and modality. The reason this was not standardized was based on the clinical situation of the patients and their family as some families travel and have long appointments, and ultrasounds could not be coordinated on the same day, so x-rays were used as a convenience to the family. However, ultrasound may be a better option for an imaging tool for screening in DS due to the lack of radiation and increased musculoskeletal detail obtained.

Down syndrome-associated arthritis (DA) remains a significant source of morbidity for children with Down syndrome (DS), there are currently no recommendations to help primary providers screen for this condition. Based on this study we propose implementation of global evidence-based education about risk of DA as part of regular anticipatory guidance given to families that have children with DS. Additionally, implementation of a brief musculoskeletal screen as part of a health screening for DS like the one in this study could be administered by providers at interval clinic visits to identify cases of inflammatory arthritis earlier. We propose focused questions about musculoskeletal health, focused musculoskeletal exam, with laboratory tests and imaging options as part of the musculoskeletal screen. Further studies are needed to improve the educational materials, the musculoskeletal screen and implement it on a larger scale.

Author Contributions

JJ, CS, and NT equally contributed to the conception, drafting, and final version of the whole manuscript. All authors read and approved the final manuscript.

Declaration of Conflicting Interests

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References

1. de Graaf G, Buckley F, Skotko BG. Estimates of the live births, natural losses, and elective terminations with

down syndrome in the United States. *Am J Med Genet A*. 2015;167A(4):756-767.
2. Asim A, Kumar A, Muthuswamy S, Jain S, Agarwal S. Down syndrome: an insight of the disease. *J Biomed Sci*. 2015;22:41.
3. Bull MJ; The Committee on Genetics. Health supervision for children with Down syndrome. *Pediatrics*. 2011;128(2):393-406.
4. Yancey CL, Zmijewski C, Athreya BH, Doughty RA. Arthropathy of Down's syndrome. *Arthritis Rheum*. 1984;27(8):929-934.
5. Foley CM, Deely DA, MacDermott EJ, Killeen OG. Arthropathy of down syndrome: an under-diagnosed inflammatory joint disease that warrants a name change. *RMD*. 2019;5(1):e000890.
6. Jones JT, Talib N, Lovell D, Becker ML. Clinical features and treatment of Down syndrome arthropathy: experience from two US tertiary hospitals. *Paediatr Drugs*. 2019;21(1):33-39.
7. Juj H, Emery H. The arthropathy of Down syndrome: an underdiagnosed and under-recognized condition. *J Pediatr*. 2009;154(2):234-238.
8. Woo P, Colbert RA. An overview of genetics of paediatric rheumatic diseases. *Best Pract Res Clin Rheumatol*. 2009;23(5):589-597.
9. Jones JT, Smith C, Becker ML, Lovell D, Investigators CR. The Down syndrome-associated arthritis cohort in the new Childhood Arthritis and Rheumatology Research Alliance (CARRA) registry: clinical characteristics, treatment and outcomes. *Arthritis Care Res*. (Hoboken). 2020 Aug 16. doi:10.1002/acr.24418. Online ahead of print.
10. Jones JT, Smith C, Talib N. Assessment of Down syndrome-associated arthritis: a survey of Down syndrome clinic providers. *Glob Pediatr Health*. 2021;8:233379 4X21999134.
11. Bull MJ. Down syndrome. *New Engl J Med*. 2020; 382(24):2344-2352.
12. Baum RA, Nash PL, Foster JE, Spader M, Ratliff-Schaub K, Coury DL. Primary care of children and adolescents with Down syndrome: an update. *Curr Probl Pediatr Adolesc Health Care*. 2008;38(8):241-261.
13. Davidson MA. Primary care for children and adolescents with Down syndrome. *Pediatr Clin North Am*. 2008; 55(5):1099-111, xi.
14. Olson JC, Bender JC, Levinson JE, Oestreich A, Lovell DJ. Arthropathy of Down syndrome. *Pediatrics*. 1990;86(6):931-936.
15. Chicoine B, Rivelli A, Fitzpatrick V, Chicoine L, Jia G, Rzhetsky A. Prevalence of common disease conditions in a large cohort of individuals with Down syndrome in the United States. *J Patient Cent Res Rev*. 2021;8(2):86-97.
16. Nicek A, Talib N, Lovell D, Smith C, Becker ML, Jones JT. Assessment and treatment of Down syndrome-associated arthritis: a survey of pediatric rheumatologists. *Pediatr Rheumatol Online J*. 2020;18(1):57.
17. Basra HAS, Humphries PD. Juvenile idiopathic arthritis: what is the utility of ultrasound? *Br J Radiol*. 2017; 90(1073):20160920.