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ORIGINAL RESEARCH

Metabolic syndrome in adults with a history of juvenile arthritis

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Objective: The objective of this study was to determine the risk of obesity and metabolic syndrome in adults with a history of juvenile arthritis (JA).

Methods: Using the National Health and Nutrition Examination Survey (NHANES), we compared the characteristics of respondents with arthritis (JA vs rheumatoid arthritis [RA]) to those of the control group without arthritis. We used logistic regression analyses, controlling for age, race, and gender, to determine the ORs for metabolic syndrome.

Results: Obesity was increased in the JA group with 67% respondents having body mass index ≥30 kg/m^2 vs 55% respondents in the no arthritis cohort (p=0.004). In unadjusted analyses, there was increased odds of metabolic syndrome in JA (OR 6.2, p=0.001) and RA groups compared to those without arthritis (OR 7.7, p=0.001). After adjusting for age, gender, and race, the odds of metabolic syndrome remained increased in JA (OR 5.2, p=0.001) and RA (OR 3.2, p=0.001) groups.

Conclusion: Adults with a history of JA have a significantly increased risk of metabolic syndrome compared to those without arthritis. These findings are important because metabolic syndrome has been associated with an increased risk of cardiovascular disease and death in other populations.

Keywords: juvenile arthritis, outcomes research, cardiovascular disease

Introduction

Juvenile arthritis (JA) is the most common chronic rheumatic disease in childhood.[1] Clinically, JA is defined as arthritis of unknown origin that manifests before the age of 16 years and persists for at least 6 weeks.[2] Although these children are known to be at risk for disease-specific complications, such as uveitis or limb length discrepancy, there are little data on long-term body composition and fitness in this cohort.

Adults diagnosed with rheumatoid arthritis (RA) are known to have an increased prevalence of metabolic syndrome defined as central obesity, dyslipidemia, hypertension, and hyperglycemia.[3–7] When the specific components of metabolic syndrome were assessed, increased waist circumference, hypertension, and high fasting glucose levels were observed in established RA patients.[6,7]

Our goal was to examine the associations of JA with obesity and risk factors for metabolic syndrome using a large panel of nationally representative data.

Methods

The National Health and Nutrition Examination Survey (NHANES) is a probability sample survey of civilians in the USA, which includes noninstitutionalized people. Data on prevalence of diseases and comorbidities are collected via interviews, physical

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examinations, laboratory tests, and radiographs. The data are freely available via the Centers for Disease Control. We linked the 2007–2014 NHANES data sets to assess the weight, body mass index (BMI), physical activity, and laboratory results of children with arthritis.[8]

Respondents with arthritis responded "yes" to the survey question: "Has a doctor or other health professional ever said you had arthritis?" We included respondents who reported RA or "other" type of arthritis; respondents with osteoarthritis and psoriatic arthritis were excluded. Our comparison group consisted of respondents who answered "no" to the arthritis survey question. We compared characteristics between respondents with arthritis, divided by age of arthritis diagnosis. JA was defined as arthritis diagnosed when ≤16 years old, and RA was defined as arthritis diagnosed when aged >16 years.[2] For the comparison group, we selected a random sample from respondents without arthritis in a 4:1 ratio to those with arthritis.

Hypertension was defined as "yes" to the survey question: "Have you ever been told by a doctor or other health professional that you have hypertension, also called high blood pressure?" Diabetes was defined as "yes" to the survey question: "Have you ever been told by a doctor or other health professional that you have diabetes or sugar diabetes?" Normal BMI was defined as per the World Health Organization as 18.5–24.9 kg/m^2, overweight as 25–29.9 kg/m^2, and obesity as ≥30 kg/m^2.[9] We also utilized the Stavropoulos-Kalinoglou cutoff classification points for BMI in RA patients for overweight as >23 kg/m^2 and obesity as >28 kg/m^2.[10] Laboratory results were obtained through NHANES sampling. Fasting blood results were reported for glucose, and results for C-reactive protein (CRP), total cholesterol, and direct high-density lipoprotein (HDL) were from nonfasting samples.

We used the US National Cholesterol Education Program Adult Treatment Panel III guidelines for metabolic syndrome, requiring at least three of the following: 1) central obesity defined as waist circumference ≥102 cm or 40 inches for males and ≥88 cm or 35 inches for females; 2) hypertension defined as blood pressure ≥130/85 mmHg (or treated for hypertension); 3) dyslipidemia defined as triglycerides ≥150 mg/dL or HDL <40 mg/dL for males and <50 mg/dL for females; and 4) fasting plasma glucose ≥110 mg/dL.[11]

We conducted analyses using Stata, version 11.2 (StataCorp LP, College Station, TX, USA) and used the survey commands provided to account for the complex sampling design. We used the NHANES sample weights that took into account the unequal selection probabilities resulting from the cluster design and planned oversampling of certain subgroups. All analyses reported incorporated these sample weights. Logistic regression analyses, controlling for age, race, and gender, were used to determine the ORs for metabolic syndrome. p-values <0.05 were considered as significant. This study was exempted from the review of the institutional review board because the data were de-identified.

Results

There were 38,909 total respondents. After the 4:1 control to arthritis random selection, there were a total of 22,807 participants in the data set. There were 232 respondents who reported a diagnosis of arthritis ≤16 years old (JA) and 1,028 randomly selected respondents with no arthritis (Table 1). At the time of the NHANES, the respondents with JA were older than those without arthritis (47.7 vs 43.7 years, p=0.001). Respondents with JA were heavier than those without arthritis (BMI 30.2 vs 28.2 kg/m^2, p=0.006), and obesity was increased in the JA group with 67% having BMI ≥30 kg/m^2 vs 55% in the no arthritis cohort (p=0.004). There was significantly more hypertension and diabetes in the JA group compared to controls. The mean duration of JA was not recorded in the NHANES. The duration of hypertension from time of diagnosis to the time of survey was increased in the JA group compared to controls (14.3 vs 10 years, p=0.002). There was no significant difference in the duration of diabetes between JA and control groups (11.9 vs 11.3 years, p=0.8).

We next compared respondents with JA to those with RA (Table 2). Despite being significantly younger at the time of the survey, respondents with JA were as obese as those with RA (79% JA vs 84% RA with BMI >28 kg/m^2, p=0.07). There was an increased prevalence of hypertension and diabetes in the RA group compared to those with JA (Table 2). There was no significant difference in the time from hypertension diagnosis to time of survey (14.3 years in the JA group vs 14.3 years in the RA group, p=0.8) and no significant difference in diabetes duration (11.9 years in the JA group vs 12.7 years in the RA group, p=0.7). As shown in Figure 1, metabolic syndrome varied by age in the different cohorts. There was no significant difference between JA and the no arthritis groups, but those with JA presented with metabolic syndrome at younger ages compared to those with RA.

We performed logistic regression analyses to determine the odds of metabolic syndrome in those with JA and RA, using those with no arthritis as the referent population (Table 3). In unadjusted analyses, there was increased odds of metabolic syndrome in those with JA (OR 6.2, p=0.001) and

Table 1 Comparison of JA and no arthritis groups

Characteristics	Arthritis dx≤16 years (n=232)	No arthritis (n=1,028)	*p*-value, arthritis dx≤16 years vs no arthritis
Current age, years	47.7	43.7	0.001
Race, %			
Caucasian	59	40	0.001
AA	22	21	
Hispanic	14	27	
Others	5	12	
Gender (female), %	59	47	0.01
Weight, kg	86.4	81.5	0.04
Height, cm	168.9	169.6	0.4
Waist/height ratio	0.6	0.5	0.001
BMI, kg/m^2	30.2	28.2	0.006
Diabetes, %	16	6	0.002
Central obesity, waist circumference ≥102 cm (male) and ≥88 cm (female), %	69	54	0.001
Hypertension (≥130/85 mmHg), %	48	24	<0.001
Low HDL (<40 mg/dL, male and <50 mg/dL, female), %	34	27	0.05
High TG (≥150 mg/dL), %	34	26	0.08
High fasting glucose (≥110 mg/dL), %	39	19	0.001
Central obesity, OR (95% CI)	1.9 (1.4–2.6)		0.001
Hypertension, OR (95% CI)	3.1 (2.3–4.2)		0.001
Low HDL, OR (95% CI)	1.3 (0.9–1.8)		0.05
Elevated TG, OR (95% CI)	1.5 (0.9–2.4)		0.08
High fasting glucose, OR (95% CI)	2.8 (1.8–4.4)		0.001

Abbreviations: AA, African American; BMI, body mass index; dx, diagnosed; JA, juvenile arthritis; HDL, high-density lipoprotein; TG, triglyceride.

Table 2 Comparison of JA and RA groups

Characteristics	Arthritis dx≤16 years (n=232)	RA (n=1,105)	*p*-value, arthritis dx≤16 years vs RA
Current age, years	47.7	58.3	0.001
Race, %			
Caucasian	59	41	0.001
AA	22	31	
Hispanic	14	23	
Others	5	5	
Gender (female), %	59	61	0.7
Weight, kg	86.4	84.2	0.2
Height, cm	168.9	164.9	0.005
Waist/height ratio	0.6	0.6	0.4
BMI, kg/m^2	30.2	30.7	0.6
Central obesity, waist circumference ≥102 cm (male) and ≥88 cm (female), %	69	73	0.2
Hypertension (≥130/85 mmHg), %	48	56	0.01
Diabetes, %	16	22	0.01
Low HDL (<40 mg/dL, male and <50 mg/dL, female), %	34	33	0.8
High TG (≥150 mg/dL), %	34	30	0.4
High fasting glucose (≥110 mg/dL)	39	37	0.8
Central obesity, OR (95% CI)	0.8 (0.6–1.1)		0.2
Hypertension, OR (95% CI)	0.7 (0.5–0.9)		0.004
Low HDL, OR (95% CI)	1.1 (0.8–1.4)		0.8
Elevated TG, OR (95% CI)	1.2 (0.8–1.9)		0.4
High fasting glucose, OR (95% CI)	1.1 (0.7–1.6)		0.8

Abbreviations: JA, juvenile arthritis; RA, rheumatoid arthritis; AA, African American; BMI, body mass index; dx, diagnosed; HDL, high-density lipoprotein; TG, triglyceride.

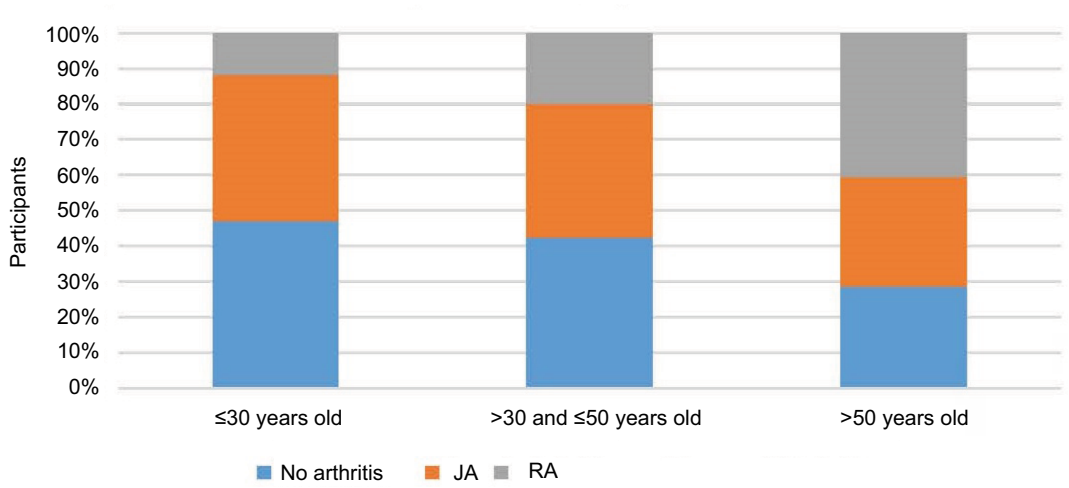

Figure 1 Prevalence of metabolic syndrome by age and diagnosis.
Notes: There was no significant difference between no arthritis and JA groups. The JA cohort had a younger age of presentation of metabolic syndrome compared to the RA cohort.
Abbreviations: JA, juvenile arthritis; RA, rheumatoid arthritis.

Table 3 Odds of metabolic syndrome in JA and RA groups compared to the no arthritis group

Odds ratio	Arthritis dx≤16 years vs no arthritis		RA vs no arthritis	
	Logistic regression, 95% CI	*p*-value	Logistic regression, 95% CI	*p*-value
Not adjusted	6.2 (3.1–12.6)	0.001	7.7 (5.1–11.8)	0.001
Adjusted for age, gender, and race	5.2 (2.3–11.9)	0.001	3.2 (1.9–5.2)	0.001

Abbreviations: JA, juvenile arthritis; RA, rheumatoid arthritis.

RA compared to controls (OR 7.7, p=0.001). After adjusting for age, gender, and race, the odds of metabolic syndrome remained increased in those with JA (OR 5.2, p=0.001) and RA (OR 3.2, p=0.001).

We explored possible reasons for the increased obesity found in the JA group. There was no significant difference in physical activity between groups (3.7 days/week in the JA group, 3.3 days/week in the no arthritis group, and 3.6 days/week in the RA group, p=0.2). A surrogate for inflammation, CRP level, was collected from respondents during NHANES years 2007–2008 and 2009–2010. Respondents with JA had higher mean CRP levels compared to those without arthritis (0.6 mg/dL vs 0.3 mg/dL, p=0.001), but there was no significant difference between JA and RA groups (0.6 mg/dL vs 0.7 mg/dL, p=0.5).

Discussion

In this study, using the NHANES 2007–2014 annual survey data, we have shown that respondents with JA have increased odds of metabolic syndrome as well as increased obesity, waist circumference, hypertension, and diabetes compared to respondents without arthritis.

Several studies have demonstrated that children with JA have high obesity rates with increased fat mass compared to healthy age-matched peers.[12,13] The etiology of this increased obesity is thought to be multifold with decreased physical activity, glucocorticoids, and increased disease activity all contributing.[12–14] Our analyses have shown that this increased obesity persists into adulthood, despite adequate physical activity.

In the current study, only 37% of JA respondents had obtained CRP levels, but the trend showed increased levels compared to those without arthritis. In women with RA, increased truncal fat has been associated with elevated CRP levels.[15] This suggests that the trend of elevated CRP in JA noted in this study could be due to inherent inflammation or adiposity rather than complications from medication use.

In patients with RA, obesity is common.[4–7,15,16] Increased inflammatory cytokines can also lead to changes in body composition such as loss of muscle mass and concomitant increase in fat mass, particularly abdominal adiposity.[15] In our study, the respondents with JA had increased waist/height ratios compared to those without arthritis, but there was no significant difference between RA and JA respondents. This is concerning because of the known risk of abdominal fat with cardiovascular disease. In a report by Giles et al,[16] higher levels of visceral abdominal fat in RA patients were associated with cardiometabolic risk factors including elevated fasting glucose, hypertension, and metabolic syndrome.

Our study has several limitations. NHANES uses patients' self-reported diagnoses that may be an inaccurate way to define medical conditions, since a proportion of individuals may not seek medical care; therefore, these individuals may be underdiagnosed and uncounted in the final analyses. This is a concern for patients with few or no symptoms who may not yet be diagnosed with hypertension or metabolic syndrome. NHANES does not collect data on arthritis activity or joint exam, and we found no JA participants taking prednisone, methotrexate, or TNF alpha therapy. This raises a limitation of the accuracy of the information, either in diagnosis or treatment. Participants who reported a previous diagnosis of JA or RA may have been misdiagnosed by other health professionals. It has been reported that a diagnosis of RA by a primary care physician is often modified once evaluated by a rheumatologist.[17] Misclassification or recall bias may affect both the age and type of arthritis classification, impacting the numbers of respondents in each group. The strengths of our study include the use of the NHANES data set, which is based on a large, nationally representative survey of the US adult population.

Conclusion

We found that adults with a history of JA have sixfold increased risk of metabolic syndrome compared to those without arthritis. These findings are important because metabolic syndrome has been associated with an increased risk of cardiovascular disease and death in other populations, and adults with JA should be monitored closely for these complications.

Acknowledgments

The authors confirm that this manuscript has not been submitted elsewhere and that no portion of the data has been or will be published in proceedings or transactions of meetings or symposium volumes.

Author contributions

All authors contributed toward data analysis, drafting and revising the paper and agree to be accountable for all aspects of the work.

Disclosure

The authors report no conflicts of interest in this work.

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