Contents lists available at ScienceDirect

Journal of Microbiology, Immunology and Infection

Journal homepage: http://www.e-jmii.com

Original Article

Nutritional Status and Clinical Characteristics in Children With Juvenile Rheumatoid Arthritis

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BACKGROUND/PURPOSE: The aim of the study was to investigate the clinical characteristics and nutritional status of juvenile rheumatoid arthritis (JRA) in Taiwanese children.

METHODS: Fifty-three patients were included in this study. The disease subtype and patient characteristics were recorded. Body mass index (BMI) was determined. Seventy-five healthy age-matched children served as a control group.

RESULTS: The inflammation parameters, including white blood cell count, platelet count, C-reactive protein, and erythrocyte sedimentation rate, were elevated in the systemic group. The BMI level of the JRA group was significantly lower than the control group ($p=0.006$), especially in the male patients ($p=0.016$) and when the patient age was greater than 4 ($p=0.011$). The patients with oligoarticular onset JRA had significantly lower BMI compared with the healthy control group ($p=0.012$).

CONCLUSION: Nutritional status is often impaired in patients with JRA. The BMI of the JRA patients was lower than that of age-matched healthy children, especially in the male group, and when disease onset age was greater than 4. In our unselected sample, the most affected disease subtype was oligoarticular onset JRA.

KEYWORDS: body mass index, juvenile rheumatoid arthritis, nutritional status

Introduction

Juvenile rheumatoid arthritis (JRA) is one of the most common pediatric rheumatic diseases, with peak age at 4 and 10 years.[1] It is a heterogeneous group of conditions of unknown etiology, each of which has specific clinical features and prognostic implications.[2] It is one of the major causes of short- and long-term morbidity, and growth impairment is one of the complications, especially in polyarticular and systemic JRA.[3] Poor nutritional status has also been reported in adult rheumatoid arthritis patients. The body mass index (BMI) in men and women are significantly reduced in rheumatoid arthritis patients compared with controls.[4]

There are several measures which can be used to assess growth disturbance and nutritional impairment, such as height, weight, mid-upper arm circumference and the four skinfolds,[5] biochemical abnormalities,[6] and bioelectrical impedance,[7] but these measures are not optimal methods

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Article History:
Received: May 1, 2008
Revised: Dec 15, 2008
Accepted: Apr 21, 2009

for the evaluation of nutritional status in clinical practice. The BMI provides a valid measure of fatness in healthy children, and is used as a marker of nutritional status in other pediatric diseases.[8] The BMI provides an objective assessment of protein-energy depletion, or excess, and is a practical tool for routine anthropometric measures in clinics.[9]

The involvement of nutritional status (anthropometric and biochemical) has often been reported in JRA patients, but there are some discordant reports about the nutritional status and disease subtypes.[9,10] The aim of this study was to investigate the relationship between nutritional status measured by BMI, patient characteristics, and disease subtypes.

Methods

Patients

Children diagnosed with JRA and treated at National Taiwan University Hospital between 1997 and 2004 were retrospectively enrolled in this study. The diagnosis and classification of JRA were based on the 1977 American College of Rheumatology criteria.[11] The onset type was defined by the manifestations of the disease in the first 6 months after onset: polyarticular onset (=5 joints involved), oligoarthritis (=4 joints involved), and systemic onset (predominance of extra-articular features, e.g. fever and skin rash). Age at onset was defined as the age of the first physical symptoms or signs consistent with the diagnosis of JRA. BMI was recorded at a rheumatology clinic. This study included 53 JRA patients and 75 age-matched children as healthy controls. The BMI records were obtained from the healthy children who were routinely examined at each term of an elementary school in the same city, and who received scheduled vaccinations at our hospital. Informed consent and ethical approval were obtained.

Data collection

The main outcome measure used to assess nutritional status in children in this study was BMI. Patient characteristics considered as explanatory measures were age, gender, disease subtype, and duration of disease.

The laboratory parameters were white blood cell (WBC) count, platelet count, hemoglobin concentrations, C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), C3 and C4. All variables were recorded when JRA was diagnosed.

Statistical analysis

Analysis was carried out using SPSS version 13.0 (SPSS Inc., Chicago, IL, USA). The age, disease duration, and laboratory parameters are expressed as mean±standard deviation. A two-sample *t* test and one-way analysis of variance (ANOVA) were used for comparison of scores within subgroups. The body height, body weight, and BMI were expressed as the median (25^{th}–75^{th} percentile). The Mann-Whitney *U* test was used to compare the data between two groups. Differences were considered to be significant when $p \leq 0.05$.

Results

The demographic and clinical characteristics of the patients are described in Table 1. There were 23 (43.4%) patients in the oligoarticular group, 11 (20.8%) patients in the polyarticular group and 19 (35.8%) patients in the systemic group. The age of disease onset was similar between the oligoarticular and the polyarticular group, but lower in the systemic group. There was no significant difference

Table 1. Demographic and clinical characteristics of patients by disease subtype[a]

	Oligoarticular	Polyarticular	Systemic	Total	Control
No. of patients	23 (43.4)	11 (20.8)	19 (35.8)	53 (100)	75 (100)
Gender, male/female	17/6	7/4	7/12	31/22	36/39
Age when BMI recorded (yr)	9.7±3.3	9.4±3.5	6.6±3.9	8.5±3.9	8.0±2.3
Age of disease onset (yr)	8.3±3.1	8.6±4.0	5.7±4.1	7.5±3.8	–
Disease duration (mo)	16.2±13.5	9.2±10.9	10.1±9.8	12.6±12.0	–

[a]Data presented as *n* (%) or mean±standard deviation. BMI=body mass index.

of disease duration among the three disease subtypes ($p=0.151$).

A comparison of laboratory parameters by disease subtypes is summarized in Table 2. The WBC count, platelet count, level of CRP and ESR were significantly increased in the systemic form of JRA. The hemoglobin concentration was significantly lower in the systemic form of disease.

Tables 3–5 summarize the difference in body height, body weight and BMI between the different subgroups. There is no significant difference in body height and body weight among the subgroups. The BMI values are not significantly different among the three JRA subgroups ($p=0.863$, data not shown). The BMI of the total JRA group is significantly lower than the control group ($p=0.006$), but when the JRA patients and the healthy control children are divided by sex, only the male patients have lower BMI than that of the male control group ($p=0.016$). When the JRA patient and healthy children are divided into two groups by age (younger or older than 4 years of age), the JRA patients older than 4 years of age have significantly lower BMI than the healthy control group ($p=0.011$).

There is a significant difference between the BMI in the three disease subtypes and that in the healthy control

Table 2. Laboratory measurements when disease onset[a]

Parameters	Oligoarticular	Polyarticular	Systemic	*p*
WBC count ($10^3/\mu L$)	8.4±2.1	8.3±2.4	15.2±10.2	0.004
Platelet count ($10^3/\mu L$)	409±95	384±69	522±185	0.011
Hemoglobin (g/dL)	11.8±0.9	11.6±1.4	9.7±1.8	<0.001
CRP (mg/dL)	2.04±2.14	3.41±3.88	8.70±4.80	<0.001
ESR (mm/hr)	48.3±28.9	49.5±29.5	89.3±32.6	0.001
C3 (mg/dL)	156±28	147±23	175±41	0.072
C4 (mg/dL)	33±8.7	35±12.0	32±10.0	0.836

[a]Data presented as mean±standard deviation. WBC=White blood cell; CRP=C-reactive protein; ESR=erythrocyte sedimentation rate.

Table 3. Difference of body height, body weight and body mass index between patients and healthy normals[a]

Characteristics	Total JRA ($n=53$)	Control ($n=75$)	*p*
Body height (cm)	132 (111–144)	130 (125–133)	0.315
Body weight (kg)	28 (18.4–37.0)	27.8 (24.0–33.8)	0.701
BMI (kg/m^2)	15.32 (14.28–17.9)	16.9 (15.6–20.1)	0.006
Age (yr)	8.5±3.8	8.0±2.3	0.341

[a]Data presented as median (25^{th}–75^{th} percentile) or mean±standard deviation. JRA=Juvenile rheumatoid arthritis; BMI=body mass index.

Table 4. Difference of body height, body weight and body mass index between patients and healthy controls group in male and female patients[a]

Characteristics	Male			Female		
	JRA ($n=31$)	Control ($n=36$)	*p*	JRA ($n=22$)	Control ($n=39$)	*p*
Body height (cm)	137 (119–149)	130 (125–134)	0.082	121 (99–141)	130 (124–133)	0.448
Body weight (kg)	28.3 (21.6–41.2)	29.7 (24–38)	0.845	24.5 (16.5–34.7)	26.9 (22.9–31.7)	0.652
BMI (kg/m^2)	15.57 (14.5–17.9)	17.3 (15.6–20.7)	0.016	14.96 (13.90–18.02)	16.35 (15.67–18.67)	0.106
Age (yr)	8.8±4.0	8.1±2.3	0.340	8.0±3.6	7.9±2.4	0.850

[a]Data presented as median (25^{th}–75^{th} percentile) or mean±standard deviation. BMI=Body mass index.

Table 5. Difference of body height, body weight and body mass index between patients and healthy controls in different age group[a]

Characteristics	Age < 4 yr			Age > 4 yr		
	JRA (n=9)	Control (n=12)	p	JRA (n=44)	Control (n=63)	p
Body height (cm)	87 (82.5–95.7)	92 (86.8–100)	0.177	136 (120–147)	131 (127–134)	0.081
Body weight (kg)	12.5 (10.1–14.3)	13.3 (11.3–15.6)	0.337	29.9 (22.7–37.3)	29.4 (25.5–36.7)	0.692
BMI (kg/m^2)	15.10 (14.65–17.36)	15.80 (15.42–17.18)	0.136	15.72 (14.15–17.9)	17.30 (15.70–20.30)	0.011
Age (yr)	2.8±0.7	2.7±0.8	0.850	9.7±3.0	9.0±0	0.073

[a]Data presented as median (25th–75th percentile) or mean±standard deviation. BMI=Body mass index.

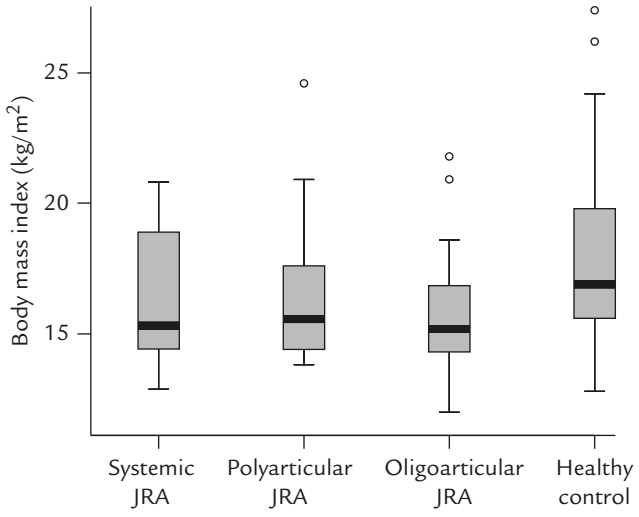

Figure. Body mass index among different disease subtypes and healthy control group. Significant different in body mass index among four groups (Kruskal-Wallis test, p=0.048) and between the oligoarticular and control group (Mann-Whitney U test, p=0.012). JRA=Juvenile rheumatoid arthritis.

group (p=0.048), and the patients with oligoarticular JRA have a significantly lower BMI compared with that of the healthy control group (p=0.012; Figure).

Discussion

In this study, boys outnumber girls in the prevalence of JRA, a finding supported by most reports from Asia.[12–14] However, this is different from most Western studies, which show a higher prevalence of JRA in girls.[15,16] The inflammation parameters, including total WBC count, platelet count, ESR and CRP were elevated in the systemic onset group. This result is also compatible with previous reports,[17–19] and indicates progressive systemic inflammation in this subtype. In our study, the BMI levels of the JRA patients were lower than those of the age-matched healthy children, especially in the male group, and those over 4 years old. In addition, the disease subtype associated with lower BMI levels was the oligoarticular onset group. The ESR and CRP levels did not correlate with the BMI within each group (data not shown).

JRA is a heterogeneous group of chronic inflammatory diseases, and poor nutritional status is often reported.[6] There are several studies suggesting that different disease subtypes and characteristics are associated with poor nutritional status, but no conclusion has been reached.[10,20–23] The poor nutritional status may be the result of (1) increased production of tumor necrosis factor-alpha and interleukin-1;[24,25] (2) decreased food intake because of chronic inflammatory disease, or a side effect of drugs; or (3) reduced physical activity.[26] Poor nutritional status may affect the general well-being of the diseased child, and contribute to growth disturbance.[9]

There is also a study showing reduced fat-free mass and a significantly higher resting energy expenditure per kilogram of body weight in patients with systemic JRA.[27] In another study, Xavier and colleagues showed that patients with a systemic, or polyarticular, disease subtype tended to present with lower percentiles of BMI.[23] It is thought that patients with systemic JRA tend to have more severe inflammation and disease activity. The nutritional status of these patients should be lower than that of the other disease subtypes and healthy controls. However, our data did not support this notion. In our study, the systemic JRA patients had more severe inflammation (higher CRP and ESR), but the BMI did not correlate with the CRP and ESR level within each subgroup. This may

suggest that, besides these inflammation factors, some undetermined factors affect the nutritional status of JRA patients. Cleary et al demonstrated that the most commonly affected subtypes were persistent oligoarthritis and rheumatoid factor-negative polyarthritis.[9] In our unselected sample, the disease subtype associated with lower BMI was oligoarthritis, and this result is compatible with the study of Cleary et al, but different from other studies. Cleary et al postulate that persistent oligoarthritis is not a disease which only affects the joints, but may also be associated with significant systemic upset and that those patients may have different cytokine profiles from those with other subtypes.[9] In the future, other cytokine profiles (including leptin) should be studied to understand why there are discordant reports about the BMI in JRA patients. More data regarding nutritional biomarkers such as serum albumin should also be collected in the future.

In our study, we also found that the male JRA patients have lower BMI levels than their corresponding age-matched healthy controls, which has not been described before. One previous study reported that male patients correlate with worse disability in systemic onset JRA, and that lower BMI may be one of the reasons.[28] In addition, a predominance of oligoarticular onset in the male group may also have some effect on the statistical results.

In the group containing children younger than 4 years old, the patients did not have lower BMI levels than the healthy controls. We chose the age of 4 as a cutoff point in this study because the BMI level dropped in the healthy controls around the age of 4. Therefore, we subdivided this group of patients to see whether there was any effect on the statistical results, but this had no effect on the results.

Pietrobelli and colleagues demonstrated that BMI is strongly associated with both total body fat and the percentage of body weight as fat in a healthy pediatric population.[5] Growth, body composition, and timing of puberty may also be abnormal in chronic inflammatory disorders. This may be a direct result of the disease, or to side effects of medication. For example, some children may become overweight when they use glucocorticosteroids for long periods. This may make the interpretation of the relationship between disease activity, or disease subtypes, and BMI more difficult.

In conclusion, the major characteristics of JRA in this study included a higher prevalence in boys, lower disease onset age in the systemic group, and elevated inflammation parameters in the systemic group. Our study also suggests that, when using BMI as measurement, impaired nutritional status has adverse effects on children with JRA (especially those with oligoarticular JRA), male patients, and those younger than 4 years-old.

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