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Body mass index is associated with health-related quality of life and disease characteristics in young adults with juvenile idiopathic arthritis

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Abstract

Background There is a growing interest concerning the relationship between obesity and several medical conditions and inflammation. Nevertheless, there is a lack of studies regarding body mass index (BMI) among patients with juvenile idiopathic arthritis (JIA). Our aim was to investigate the impact of BMI on health-related quality of life (HRQoL) measured with a 36-Item Short Form Survey (SF-36), disease activity, and disability in young adults with JIA.

Methods This study is a part of the population-based Nordic JIA cohort study. All newly diagnosed patients with JIA were recruited consecutively between 1997–2000 in specific regions in the Nordic countries. Patients in this sub-study were enrolled from 434 patients who attended their 18-year follow-up visit. Patients were classified according to the World Health Organization (WHO) into four groups based on their BMI. HRQoL, disease characteristics, disability, fatigue, sleep quality, physical activity, pain, comorbidities, and social status were assessed.

Results Three hundred fifty-five patients from the original study cohort were enrolled in this study and 72% of them were female. Mean age was 23.9 (\pm SD 4.4) years. A significant relationship was found between the JIA categories and BMI groups ($p=0.014$). A significant relationship was also found between BMI and disease activity scores (DAS28) ($p=0.028$), disability ($p<0.001$), pain ($p=0.013$), fatigue ($p=0.035$), and sleep quality ($p=0.044$). Moreover, a significant relationship between BMI and HRQoL regarding bodily pain ($p=0.010$) and general health ($p=0.048$) was revealed when adjusted for sex, age, and JIA subtype.

Conclusion We discovered that BMI was significantly related to HRQoL, disease activity, and disability. BMI deserves more attention considering the treatment options and outcome of JIA in young adults.

Keywords Body mass index, Juvenile idiopathic arthritis, Health-related quality of life, Disease activity, Disability

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Background

Juvenile idiopathic arthritis (JIA) [1] may cause various health problems during adulthood because of its chronic nature. JIA has been linked to other autoimmune diseases [2], mental health disorders [3], cardiovascular diseases [4], lower functional ability [5] and abdominal pain which is an important factor in the decreased quality of life [6].

Overweight and obesity have become increasing worldwide problems [7]. According to WHO, 39% of adults are overweight and 13% are obese [8].

The prevalence of overweight among patients with JIA is reported to be from 14.2% to 60% [9, 10]. Overweight and obesity have been associated with low-grade chronic systemic inflammation [11]. Obesity has been linked to rheumatoid arthritis (RA) [12] and especially to poor prognosis [13, 14]. To date, this topic is relatively little studied among young adults with JIA. Moreover, higher prevalence of overweight and obesity has been linked to autoimmune diseases among children and adolescents [15].

There is a lack of studies on body mass index (BMI) and JIA in young adults. Our aim was to study the impact of BMI on HRQoL and disease parameters among young adults with a JIA diagnosis.

Methods

This study is part of the population-based Nordic JIA cohort study [16, 17]. All newly diagnosed patients with JIA were recruited consecutively between 1997–2000 in specific regions in the Nordic countries (Finland, Sweden, Norway, and Denmark). Patients in this sub-study were enrolled from 434 patients who attended their 18-year follow-up visit [16]. Seventy-five patients of the 434 were excluded because of missing data on either height, weight, or both. Consequently, 355 (82%) patients were eligible for this study.

BMI was categorized into four groups: BMI < 18.5 (underweight), BMI 18.5–24.9 (normal weight), BMI 25–29.9 (overweight) and BMI ≥ 30 (obesity) [18].

Children's and adolescents' (2–18 years) age- and sex-adjusted BMI was converted to ISO-BMI to correspond to an adult BMI by an age-appropriate factor. ISO-BMI < 17 (underweight), ISO-BMI 17–24.9 (normal weight) and ISO-BMI 25–29.9 (overweight) and ISO-BMI ≥ 30 (obesity) [19].

The SF-36 was used to evaluate the Health-Related Quality of Life (HRQoL) of the patients. The SF-36 includes eight domains measuring physical functioning, role limitation due to physical problems, bodily pain, general health perception, vitality, social functioning, role limitation due to emotional problems and mental health. Each domain is scored on a scale of 0–100. Zero

represents the worst health status and 100 the best overall health status [20, 21].

The disease activity was evaluated by the Disease Activity Score in 28 joints (DAS28) [22]. DAS28 scales from 0 to 9.4; < 2.6 indicating remission, 2.6–3.2 low disease activity, 3.2–5.1 moderate disease activity and > 5.1 very high disease activity [23].

Functional ability was assessed by the Health Assessment Questionnaire (HAQ) [24]. The Wallace criteria were used to define remission [25]. Pain intensity was scored by the patient on a visual analogue scale (VAS), with 0 indicating no pain and 100 the worst possible pain.

Self-reported fatigue was assessed by the Fatigue Severity Scale (FSS, 0–7) [26]. Higher values indicate more severe fatigue. Information on sleep quality was evaluated with the Pittsburgh Sleep Quality Index (PSQI) comprising of seven categories: sleep duration, sleep disturbance, sleep latency, daytime dysfunction due to sleepiness, sleep efficiency, sleep quality, and use of sleep medication. The total score ranges from 0 to 21, with higher scores indicating poorer sleep quality [27].

Physical activity was assessed by asking questions on the frequency, intensity, and duration of exercise based on the Kasari-FIT index [28]. The score is 1–100, and a higher score indicates higher physical activity (0–12 insufficient amount, 13–36 moderate amount, 37–63 good amount and 64–100 excellent amount of exercise). The Kasari-FIT index was evaluated subsequently using the information collected at the 18-year study point. Exercise habits were assessed with the Frequency-Intensity-Time (FIT) Index [28].

Abdominal pain was classified into three categories according to the frequency: (1) never (2) seldom (one to three times a month) and (3) frequent (at least once a week).

Comorbidities, such as autoimmune thyroiditis and inflammatory bowel disease (IBD) were registered at the visit. Information on student and employment status as well as present medications were registered.

Approval for this study had been obtained from the local medical ethics committees. Informed consent was requested from all participants in accordance with the rules of the participating countries.

Statistics

We present descriptive statistics as means with standard deviation (SD), and as counts with percentages. The hypothesis of linearity was tested using the Cochran–Armitage test, linear-by-linear, logistic models for categorical variables and analysis of variance (ANOVA) for continuous variables with an appropriate contrast. A possible nonlinear relationship between SF-36 dimensions and the Body Mass Index was assessed by using

3-knot-restricted cubic spline regression models; the models were adjusted for age, sex and diagnosis. The length of the distribution of knots was located at the 10th, 50th, and 90th percentiles. In the case of violation of the assumptions (e.g., non-normality) for continuous variables, a bootstrap-type method or Monte Carlo *p*-values (small number of observations) for categorical variables were used. The normality of variables was assessed graphically and by using the Shapiro–Wilk *W* test. Stata 17.0 (StataCorp LP, College Station, TX, USA) was used for the statistical analyses.

Results

This study included 355 patients from the four Nordic countries. The number of female patients was 254 (72%) and male 101 (28%), and the mean age was 23.9 (\pm SD 4.4) years. Patients were assorted according to their BMI level. Disease characteristics and additional demographic data are presented in the Table 1.

BMI

BMI was 23.8 (\pm 4.9); for females 23.5 (\pm 4.7) and males 24.6 (\pm 5.3) (Fig. 1). Six percent of the patients had BMI < 18.5 (underweight) and 11% of them had BMI \geq 30 (obesity). The BMI categories (underweight, normal weight, overweight, and obesity) remained the same as they were at baseline (Table 1).

A significant relationship was found between BMI and onset ISO-BMI. Interestingly, we noticed that the BMI categories of both underweight and obese patients remained the same at the baseline and at the follow-up visit. At the baseline, the disease activity did not differ between the BMI groups.

Clinical characteristics and outcome associated with BMI

Table 1 shows a significant association was found between the JIA categories and BMI groups. A significant relationship was found between BMI and disease activity already at the baseline. Thirty-four percent of underweight patients had persistent oligoarthritis, whereas 32% of overweight patients belonged to either the juvenile psoriatic arthritis (JPsA) or enthesitis-related arthritis (ERA) subgroup.

Higher BMI was related to disease activity according to DAS28 ($p=0.028$), lower functional ability assessed with HAQ ($p<0.001$) and to higher pain scores ($p=0.013$).

Statistically significant relationships were found between BMI and fatigue ($p=0.035$), poor sleep quality assessed with PSQI ($p=0.044$), and abdominal pain ($p<0.001$). Twenty-nine percent of patients in the obesity group reported frequent abdominal pain.

According to the Kasari FIT index, all patients in different BMI groups reported exercising moderately (Table 1).

No relationship between BMI and medication was found (Table 2). NSAIDs (Non-Steroidal Anti-Inflammatory drugs) were used by 59 patients, sDMARD (synthetic Disease Modifying Antirheumatic Drug) or bDMARD (biological Disease Modifying Antirheumatic Drug) by 103 patients, sDMARD by 70 and bDMARD by 74. In the sDMARD group, prednisolone was used by 10, methotrexate by 47, azathioprine by 4, hydroxychloroquine by 7, leflunomide by 4, sulfasalazine by 13 and cyclosporine by 3.

Health-related quality of life associated with BMI

Statistically significant relationships were detected between BMI and role limitations due to physical health ($p=0.005$), bodily pain ($p=0.021$), general health perception ($p=0.008$), and role limitations due to emotional health ($p=0.019$) (Table 3). A statistically significant relationship was found between different BMI groups and the physical component score ($p=0.011$) but not with the mental component score ($p=0.48$).

When adjusted for age, gender and JIA categories, significant relationships were revealed between BMI and continuous bodily pain ($p=0.010$) and general health ($p=0.048$) (Fig. 2); patients with healthy BMI had better quality of life.

Discussion

The main finding was that there was a significant relationship between BMI and HRQoL, highlighting that those patients with healthy BMI had better HRQoL. In addition, BMI at the 18-year follow-up visit was related to age, JIA category, disease activity, disability, pain, and student or employment status at the time of the follow-up visit, and to weight at diagnosis. Moreover, we revealed that BMI was related to fatigue and sleep quality.

Interestingly, we detected that the BMI categories of both underweight and obese patients remained unchanged at the baseline and at the follow-up visit. At the baseline, the disease activity did not differ between the BMI groups.

To our knowledge, the association between BMI and HRQoL has not been previously studied in young adults with JIA. We showed that in overweight/obese patients both the physical and mental dimensions of HRQoL, including bodily pain, general health perception, the role limitations due to physical or emotional health as well as vitality were impaired. Previous studies on HRQoL have shown that patients with JIA have more restricted functional ability, and they experience more pain compared to their healthy peers [29, 30]. On the other hand, it has been reported that adult patients with persistent oligoarthritis and ERA have a better HRQoL compared to the other JIA subgroups [31].

Table 1 Disease characteristics according to BMI groups in the 18-year follow-up visit

	< 18.5 N=21	18.5-24.9 N=237	25.0-29.9 N=59	≥ 30.0 N=38	P value*
Female, n (%)	15(71)	173(73)	42(71)	24(63)	0.30
Age at onset, years, mean (SD)	4.0(3.2)	6.1(4.1)	7.8(3.8)	7.9(3.9)	< 0.001
Symptom duration, months, mean (SD)	8(16)	5(8)	7(9)	5(7)	0.95
ISO-BMI at onset, (z-score) mean (SD)	-1.51(3.69)	1.08(3.24)	2.39(2.93)	3.10(2.32)	< 0.001
JADAS at onset	2.2(3.6)	2.0(3.6)	1.9(3.3)	2.0(2.8)	0.80
Age	20.8(4.0)	22.9(4.4)	24.7(4.2)	25.2(4.3)	< 0.001
Disease duration	16.5(2.9)	16.7(1.6)	16.6(1.4)	17.1(1.0)	0.24
Subgroup of JIA, n (%)					0.014
Persistent oligoarthritis	9(43)	66(28)	10(17)	6(16)	
Extended oligoarthritis	3(14)	58(24)	10(17)	4(11)	
Polyarthritis, RF-positive	1(5)	2(1)	1(2)	2(5)	
Polyarthritis, RF-negative	5(24)	42(18)	10(17)	4(11)	
Psoriatic arthritis	1(5)	7(3)	4(7)	6(16)	
Enthesitis-related	0(0)	21(9)	8(14)	6(16)	
Systemic onset	0(0)	11(5)	2(3)	0(0)	
Undifferentiated	2(10)	30(13)	14(24)	10(26)	
DAS28	1.92(0.97)	1.83(0.86)	1.91(0.97)	2.26(1.01)	0.028
Tender joints 28	1.3(2.0)	0.6(1.7)	0.9(2.1)	1.9(4.3)	0.019
Swollen joints 28	0.5(0.7)	0.3(1.1)	0.5(1.5)	0.3(1.2)	0.92
Patients' global, VAS	20.5(24.5)	14.7(22.7)	26.2(29.9)	29.3(33.8)	< 0.001
ESR	5.5(4.8)	6.7(6.8)	7.6(6.7)	12.3(9.6)	< 0.001
CRP	3.8(2.5)	2.8(3.7)	3.7(3.9)	7.2(8.3)	< 0.001
HAQ	0.15(0.35)	0.13(0.31)	0.33(0.59)	0.38(0.65)	< 0.001
Remission					0.17
No remission	14(67)	110(46)	24(41)	21(55)	
Remission on medication	0(0)	26(11)	3(5)	4(11)	
Remission off medication	7(33)	101(43)	32(54)	13(34)	
Pain, VAS	26.0(27.8)	15.8(22.0)	24.5(27.7)	28.1(29.9)	0.013
Fatigue total, mean (SD)	3.0(1.6)	3.1(1.5)	3.5(1.7)	3.6(1.6)	0.035
PSQI, mean (SD)	5.4(2.7)	5.5(3.4)	6.0(4.1)	6.8(4.1)	0.044
Kasari FIT-index	29.0(20.9)	33.9(23.2)	35.5(21.8)	28.8(19.2)	0.68
Abdominal pain					< 0.001
No	17(81)	197(83)	42(71)	24(63)	
Sometimes	3(14)	25(11)	8(14)	3(8)	
Always	1(5)	15(6)	9(15)	11(29)	
Comorbidities					
Hypothyreosis	0(0)	6(3)	2(3)	0(0)	0.78
IBD	2(10)	7(3)	1(2)	1(3)	0.30
Social status					0.004
Student	10(48)	119(50)	27(46)	9(24)	
Employed	6(29)	108(46)	29(49)	22(58)	
Unemployed	3(14)	5(2)	1(2)	1(3)	
On pension	2(10)	5(2)	2(3)	6(16)	

ISO-BMI Body Mass Index

JADAS Juvenile Arthritis Disease Activity Score

JIA Juvenile idiopathic arthritis

RF Rheumatoid Factor

DAS28 Disease Activity Score 28

ESR Erythrocyte Sedimentation Rate

CRP C-reactive protein

HAQ Health Assessment Questionnaire

VAS Visual Analogue Scale

PSQI Pittsburgh Sleep Quality Index

IBD Irritable Bowel Disease

* P value for linearity across the three BMI levels

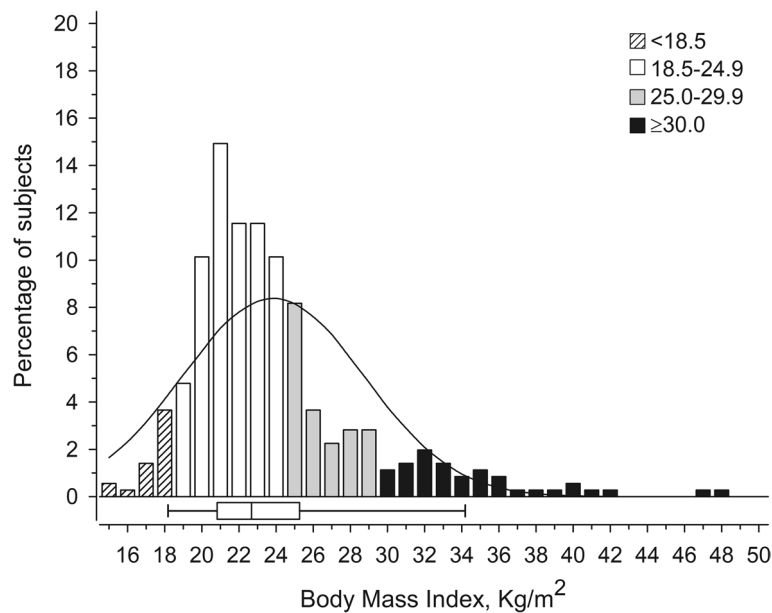


Fig. 1 Distribution with normal curve overlay of BMI in the 18-year follow-up visit. Box-and-whiskers plot shows median and IQR, and whiskers indicate 5th and 95th percentiles

Table 2 Medication according to BMI groups in the 18-year follow-up visit

Medication	< 18.5 N=21	18.5-24.9 N=237	25-29.9 N=59	≥ 30.0 N=38	P value*
NSAIDs	1(5)	39(16)	10(17)	9(24)	0.15
sDMARD or bDMARD	7(33)	71(30)	15(25)	13(34)	0.99
sDMARD	5(24)	48(20)	9(15)	8(21)	0.66
bDMARD	5(24)	50(21)	11(19)	8(21)	0.76
prednisolone	1(5)	7(3)	2(3)	0(0)	0.47
methotrexate	2(10)	34(14)	5(8)	6(16)	0.99
azathioprine	1(5)	2(1)	0(0)	1(3)	0.99
hydroxychloroquine	0(0)	6(3)	1(2)	0(0)	0.99
leflunomide	1(5)	3(1)	0(0)	0(0)	0.16
sulfasalazine	0(0)	8(3)	4(7)	1(3)	0.60
cyclosporine	1(5)	1(0)	1(2)	0(0)	0.87

NSAIDs Non-Steroidal Anti-Inflammatory Drugs

sDMARD synthetic Disease Modifying Antirheumatic Drug

bDMARD biologic Disease Modifying Antirheumatic Drug

* P value for linearity across the three BMI levels

We found that BMI was associated with disease activity as measured by the DAS28. This association has been relatively little studied in JIA or in rheumatic diseases overall. A previous study suggests that obesity has a negative influence on the disease course and in the treatment response in JIA [32]. Excess adipose tissue can alter the pharmacokinetics of biological drugs and therefore diminish the treatment response [33]. This was also confirmed by a recent study in patients with psoriatic arthritis (PsA) [34]. Furthermore, ambivalent results

have been revealed: no association between obesity and disease activity among patients with JIA in one study [35] and another study showed an association between underweight and higher disease activity [36].

Previously, it has been shown that growth and weight gain among children with JIA were comparable to the general population [37]. Children at risk of poor growth had systemic arthritis, uncontrolled disease and/or long-term use of corticosteroids [37]. A study from India showed that the weight, height, BMI, and growth velocity

Table 3 Quality of Life according to BMI groups in the 18-year follow-up visit

	< 18.5 N = 21	18.5-24.9 N = 237	25.0-29.9 N = 59	≥ 30.0 N = 38	P value*
SF-36					
Physical functioning	83(24)	90(18)	86(21)	85(20)	0.32
Role limitations due to physical health	83(30)	84(32)	76(39)	67(43)	0.005
Bodily pain	68(27)	76(23)	70(26)	64(27)	0.021
General health perceptions	67(25)	69(26)	63(26)	56(26)	0.008
Vitality	50(20)	60(24)	53(24)	52(25)	0.077
Social role functioning	76(27)	87(20)	82(25)	82(27)	0.48
Role limitations due to emotional health	81(36)	84(31)	77(37)	69(41)	0.019
Mental health	66(23)	76(17)	74(21)	74(20)	0.81
Summary scores					
Physical Component Score	51(9)	52(10)	50(11)	48(11)	0.011
Mental Component Score	45(11)	50(11)	48(13)	48(12)	0.48

SF-36 36-Item Short Form Survey

* P value for linearity across the three BMI levels

of children with JIA was reduced compared to controls [38]. RA patients that were overweight at the time of diagnosis were found to have a higher disease activity and they experienced more pain at the beginning of the disease [39].

In our study, we found an association between BMI and disability. This is consistent with a meta-analysis [40] showing that excessive body fat has an unfavourable effect both in the disease activity as well as in the functional ability of patients with RA, but others have shown contradictory results [41].

Obesity and JIA as individual factors have been linked to more pain in adolescence [42, 43]. Early self-reported pain in JIA has been found to predict persistent and unfavourable long-term disease outcome [44]. Previously, it has been shown that JPsA [45], ERA and undifferentiated JIA [46] patients experience more pain compared to other JIA subgroups. In our study, the patients in the obesity group reported significantly more pain than other BMI groups.

In previous studies obesity has been associated with higher inflammatory values in RA patients [47]. In our study we found that patients with higher BMI also had higher CRP and ESR. It remains to be clarified whether inflammatory values were elevated due to rheumatic inflammation or because of obesity. Earlier, it has been shown that high levels of inflammatory markers are related to adipose tissue and not to the disease activity in RA [47]. On the other hand, the central adiposity manifested in obesity may contribute to a persistent low-grade inflammation in patients with JIA [48]. In a Finnish study, although children with JIA had low disease activity, they had higher central adiposity compared to healthy controls [49].

Thirty-two percent of overweight patients in our study belonged to either the PsA or ERA subgroup. Previous studies are in line with our findings showing the association between obesity and different rheumatic disease categories in adults, such as PsA and RA [50, 51]. Obesity is among the most common comorbidities in patients with PsA [52, 53] and the prevalence of obesity was reported to be 44% [54]. Similarly, juvenile ERA patients were most likely to be overweight compared to other JIA categories [9].

Available data suggests that patients with JIA or RA experience more sleep disturbances and sleep less compared to their healthy peers, and they report more fatigue [55–57]. Adequate amount of sleep has many beneficial effects in children and adolescents [58]. Instead, short sleep duration is connected to excess fat accumulation, it impairs academic coping and is associated with lower QoL and emotional challenges [59]. Our study revealed that higher BMI was associated with fatigue and poor sleep quality, and, intriguingly, underweight patients had the best sleep quality, and they reported less fatigue. In line with our findings is a study that showed the association of overweight and obesity with poor sleep quality and short sleep duration [60]. Obesity, overweight and underweight were all associated with short sleep duration [61]. Moreover, poor sleep quality has other unfavourable effects, and it also causes constant low-grade inflammation [62]. Poor sleep together with depression is relatively common in arthritis patients [63].

Physical activity has many beneficial effects on general well-being, and mental and physical health [64–66]. Studies show that especially patients with JIA or RA benefit from physical activity [66], but JIA patients were found to be less active than their healthy peers [67]. A

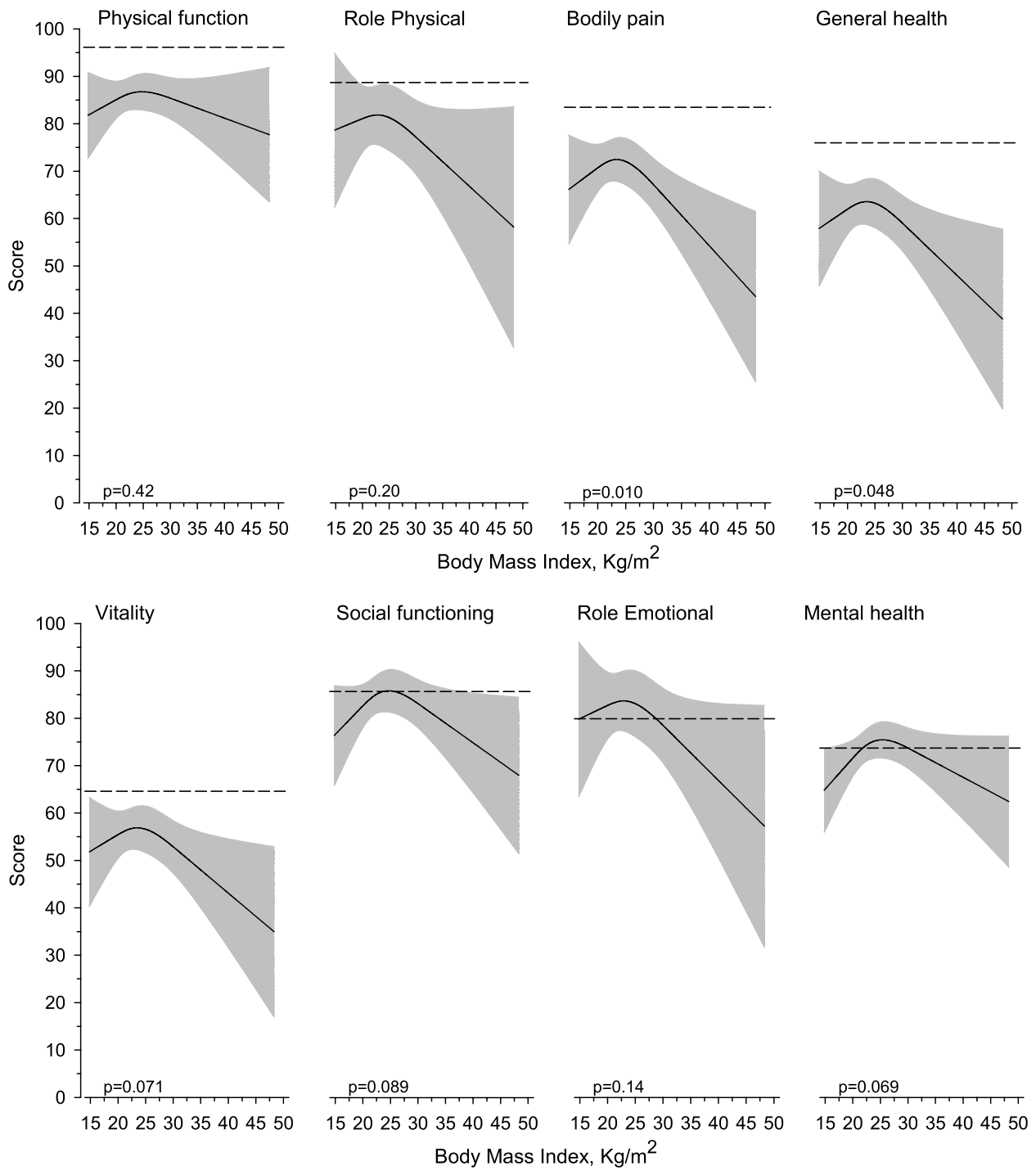


Fig. 2 Relationships of dimensions of health-related quality of life as the function of the BMI in the 18-year follow-up visit. The curves were derived from 3-knot restricted cubic splines regression models. The models were adjusted for age, sex and diagnosis. The grey area represents a 95% confidence interval. Age- and gender-matched healthy controls from the study by Aalto et al. [21] shown by the dashed lines

lower level of physical activity was found to be associated with overweight in patients with JIA [9, 65, 66]. From the very onset of JIA, children should be encouraged to take part in physical activity as the JIA diagnosis should not

be a complete barrier to sports [68]. In this study we did not find a particularly low level of physical activity in any BMI group, and on average the levels of physical activity were eligible according to the Kasari-FIT [28].

Our study has several strengths. This study is long-term and prospective in its origin, and to our knowledge is the first study investigating the relationship between BMI and HRQoL in adult patients with JIA.

The minor limitation of the study is caused by the questionnaire-based and partially self-reported data by the patients including some missing data because of the long-term nature of the study. A limitation is also the absence of the control group. The study is based on a Nordic cohort and all new JIA cases were included, but it can be demanding to make broad generalizations based on these study results.

Conclusions

Our novel findings suggest that BMI level should be acknowledged by healthcare professionals taking care of patients with arthritis. Based on our main findings we conclude that BMI and especially obesity impairs the HRQoL of adult patients with JIA. The patients should be encouraged to carry out physical activity together with weight control because of the versatile effect on general well-being. Based on our findings and previous data, we also recommend that sleep quality should be routinely assessed.

Abbreviations

BMI	Body mass index
JIA	Juvenile idiopathic arthritis
HRQoL	Health-related quality of life
SF-36	36-Item Short Form Survey
WHO	World Health Organization
DAS28	Disease Activity Score 28
RA	Rheumatoid arthritis
HAQ	Health Assessment Questionnaire
VAS	Visual Analogue Scale
FSS	Fatigue Severity Scale
PSQI	Pittsburgh Sleep Quality Index
FIT	Frequency-Intensity-Time
IBD	Inflammatory bowel disease
SD	Standard deviation
ANOVA	Analysis of variance
JPsA	Juvenile psoriatic arthritis
ERA	Enthesitis-related arthritis
NSAIDs	Non-Steroidal Anti-Inflammatory Drugs
sDMARD	Synthetic Disease Modifying Antirheumatic Drug
bDMARD	Biologic Disease Modifying Antirheumatic Drug
JADAS	Juvenile Arthritis Disease Activity Score
RF	Rheumatoid Factor
ESR	Erythrocyte Sedimentation Rate
CRP	C-reactive protein

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Authors' contributions

The first draft of the manuscript was written by Anna-Kaisa Tuomi and Katariina Rebane. Anna-Kaisa Tuomi, Katariina Rebane, Hannu Kautiainen, and Kristiina Aalto contributed to the study design and in statistical analysis interpretation of the data and preparing the manuscript. All the authors participated in collecting data and revised the final version of the manuscript.

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Availability of data and materials

The data are not publicly available for ethical and privacy reasons but are available by an appropriate permission request.

Declarations

Ethics approval and consent to participate

The study was approved by Ethics Boards at all participating countries and performed in accordance with the Declaration of Helsinki, including informed written consent.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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