

# *Metabolic syndrome and juvenile idiopathic arthritis*

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## ABSTRACT

Juvenile idiopathic arthritis (JIA) is the most prevalent chronic arthropathy in childhood and adolescence. The prevalence of metabolic syndrome, as well as obesity, is increasing rapidly in all age groups, including children. Metabolic syndrome is defined as a cluster of risk factors for cardiovascular disease and type 2 diabetes mellitus, including abdominal obesity, insulin resistance, dyslipidemia and hypertension. Besides those components, inflammation has been increasingly considered as a significant component of metabolic syndrome and obesity, and patients with diseases characterized by the presence of chronic inflammation, such as JIA, could represent special risk groups. Glucocorticoids are used routinely in the management of the inflammation of JIA, in high doses and long-term. Long-term use of the glucocorticoids can cause to insulin resistance, hypertension, and obesity, increasing the risk of metabolic syndrome. The aim of this study is to review the literature on the prevalence of different components of metabolic syndrome in patients with JIA. We observed that the data on metabolic syndrome and its components in those patients are very scarce and more studies needed, in view of the potential increased risk of cardiovascular disease.

**Keywords:** juvenile idiopathic arthritis, metabolic syndrome, obesity.

## INTRODUCTION

Juvenile idiopathic arthritis (JIA) is a chronic arthropathy more prevalent in childhood and adolescence. The term describes a heterogeneous group of childhood disorders with chronic inflammation in one or more joints. The onset of JIA is before 16 years of age. Prevalences ranging from 16 to 150/100,000 have been reported in the general population.<sup>1</sup> The absence of studies on JIA patients in the Brazilian is responsible for the lack of knowledge on the prevalence and incidence of this disorder in our country.

Metabolic syndrome (MetS) is characterized by the presence of a cluster of metabolic abnormalities, especially overweight, abdominal obesity, insulin resistance (IR), dyslipidemia, and hypertension,<sup>2-4</sup> and it has become increasingly more important due to the association with the development of cardiovascular diseases (CVD) and type 2 diabetes mellitus (T2DM) in adults.<sup>3</sup>

Metabolic syndrome in adults has several definitions, but that of the National Cholesterol Education Program's Adult Treatment Panel III (NCEP/ATP III)<sup>4</sup>, which includes obesity, determined by measuring the abdominal circumference, hypertension, lower levels of high density lipoproteins (HDL-c), elevated triglycerides (TG), and increased fasting glucose among its diagnostic criteria, is used more often.<sup>5</sup>

The prevalence of MetS and obesity has been increasing rapidly in all age groups, including children.<sup>2,6</sup> Childhood obesity can be classified according to the criteria of the World Health Organization (WHO, 2006). Overweight is defined by the WHO as a body mass index (BMI) (in kilograms divided by the square of the height) between the 85<sup>th</sup> and 97<sup>th</sup> percentile, and obesity is defined as a percentile  $\geq 97$  for age and gender.<sup>7</sup> However, a diagnostic consensus for MetS in the pediatric population<sup>3</sup> does not exist, and the criteria used by different studies have been adapted from adult patterns, using levels dependent on gender and age.<sup>6</sup>

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Recently, the International Diabetes Federation (IDF) published its definition of MetS in children and adolescents. The recommendation includes the following criteria: for children between 6 and < 10 years, obesity is defined as percentile  $\geq 90$  and other evaluations can be done in the presence of family history of MetS, T2DM, dyslipidemia, CVD, and hypertension. For children between 10 and < 16 years, obesity is defined as percentile  $\geq 90$ , following adult criteria for the levels of TG, HDL-c, blood pressure, and glucose. For adolescents > 16 years, the IDF recommends the use of the definition of MetS established for adults.<sup>8</sup>

Other studies define MetS in childhood using criteria proposed by the NCEP/ATP III, with the presence of three of the following criteria:<sup>5</sup> BMI  $\geq 97^{\text{th}}$  percentile, TG  $\geq 110$  mg/dL, HDL-c  $\leq 40$  mg/dL, waist circumference above the 90<sup>th</sup> percentile (age and gender), glucose levels > 100 mg/dL and  $\geq 95^{\text{th}}$  percentile (age, gender, and height)<sup>9,10</sup> (Table 1). The determination of insulin resistance (IR) and C-reactive protein (CRP) levels also been reported in studies on MetS and CVD, since the evidence suggests that IR and inflammation could be related with cardiovascular risk.<sup>11,12</sup>

The role of inflammation on MetS has been increasingly demonstrated.<sup>13</sup> Different pro and anti-inflammatory cytokines, the main regulators of the inflammatory process, induce its effects individually or by interacting with each other. In JIA, studies have demonstrated an imbalance favoring the production of pro-inflammatory cytokines, including interleukin-1 $\beta$  (IL-1 $\beta$ ), interleukin-6 (IL-6), and tumor necrosis factor-alpha (TNF $\alpha$ ), that are important contributors to the perpetuation of the inflammatory response.<sup>14</sup> Patients with chronic inflammatory diseases have a higher risk of premature CVD.<sup>15</sup>

Glucocorticoids are used routinely in the management of the inflammation of JIA, in high doses and long-term. In the past few

years, it has been observed that the chronic use of glucocorticoids could lead to IR,<sup>16</sup> hypertension, and obesity, all components of the MetS.<sup>17</sup> Besides, the presence of chronic inflammation in JIA could be added as a cardiovascular risk factor.

Our group studied the nutritional status in 116 JIA patients and the use of glucocorticoids, and found that 23.3% of the patients were overweight.<sup>18</sup> However, the prevalence of MetS and obesity were not evaluated in this study.

We carried out a review of the current literature on the investigation of MetS, how this disorder develops in childhood and adolescence, its relationship with long-term use of glucocorticoid and chronic inflammation, and potential consequences in JIA patients. The following descriptors were used in the literature search: juvenile idiopathic arthritis, metabolic syndrome, obesity, glucocorticoids, and inflammation in the MEDLINE and LILACS databases, as well as the 2009 EULAR and ACR congresses.

## METABOLIC SYNDROME

It has been estimated that the prevalence of MetS has been increasing in the pediatric population. However, there is no standardisation of the diagnostic criteria for MS. Epidemiological studies on MetS, using different criteria, have been published recently, but interpretation of the results is hindered due to the lack of consensus on the definition and cut points of its components.<sup>3,4,9</sup>

According to the definition criteria in children and adolescents, it has been estimated that more than one million American adolescents meet the ATP III criteria for the MetS.<sup>2</sup> Among published studies, the prevalence of MetS varies from 3 to 42%, with a high prevalence in obese children<sup>4,9,19-24</sup> (Table 2). According to the Third National Health and Nutrition and

**Table 1**  
Parameters of the Metabolic Syndrome in Children and Adolescents

Parâmetros	ATPIII	IDF (10 a 16 anos)*	NHANES III
# of risk factors	$\geq 3$	$\geq 2$	Todas
Waist circumference		$\geq$ percentile 90	$\geq$ percentile 90
Triglycerides	$\geq$ percentile 95	$\geq 150$ mg/dL	$\geq 110$ mg/dL
HDL	> percentile 5	< 40 mg/dL	$\leq 40$ mg/dL
Glucose	TGC	$\geq 110$ mg/dL	$\geq 110$ mg/dL
Blood pressure			
Systolic	> percentile 95	> 130 mmHg	
Diastólica	> percentile 95	$\geq 85$ mmHg	

ATPIII: Adult Treatment Panel; IDF: International Diabetes Federation; NHANES III: National Health and Nutrition Examination Survey. IGT: impaired glucose tolerance; \* For Children older than 16 years, the IDF adult criteria can be used.

**Table 2**  
Prevalence of the Metabolic Syndrome (MetS) in Children and Adolescents

Author and year	Study	Population	Age (years)	Definition criteria of MetS	Prevalence of MetS
Cook <i>et al.</i> , 2003 <sup>9</sup>	Transversal Data NHANES 1988-1994	2,430	12 to 19	NHANES III	4.2%
Ford <i>et al.</i> , 2005 <sup>19</sup>	Transversal Data NHANES 1999-2000	1,366	12 to 17	NHANES III (TGC)	5.2%
Ford <i>et al.</i> , 2008 <sup>20</sup>	Transversal Data NHANES 1999-2004	2,014	12 to 17	IDF	4.5%
Johnson <i>et al.</i> , 2009 <sup>21</sup>	Transversal Data NHANES 2001-2006	2,456	12 to 19	NHANES III (glucose $\geq$ 100 mg/dL)	8.6%
Weiss <i>et al.</i> , 2004 <sup>22</sup>	Cohort	490	4 to 20	ATPIII (IGT $>$ 140 mg/dL* or HOMA-IR $>$ 15)	38.7% moderate obesity and 49.7% severe obesity
Ferreira <i>et al.</i> , 2007 <sup>23</sup>	Transversal	52	7 to 10	NHANES III /ATPIII (BMI $\geq$ percentile 95*, HDL $\leq$ 38 mg/dL, glucose $\geq$ 126 mg/dL and IR)	17.3% in obese patients
Buff <i>et al.</i> , 2007 <sup>24</sup>	Transversal	50	2 to 10	NHANESIII (glucose $\geq$ 100 mg/dL)	42.3% obese patients
Strufaldi <i>et al.</i> , 2008 <sup>4</sup>	Transversal	929	6 to 10	(BMI $\geq$ percentile 95*, TG $\geq$ 130 mg/dL and HDL $\leq$ 40 mg/dL, glucose $\geq$ 100 mg/dL or IR $>$ 3.1 and BP $\geq$ percentile 95**)	MetS/ATPIII 9.3% MetS/WHO 1.9%

NHANES: National Health and Nutrition Examination Survey; IDF: International Diabetes Federation; ATPIII: Adult Treatment Panel; WHO: World Health Organization; CGT: compromised glucose tolerance; HOMA-IR: Homeostasis Model Assessment - Insulin Resistance; IR: insulin resistance; BMI: body mass index; HDL: high-density lipoprotein; TG: triglycerides; BP: blood pressure. \*age and gender; \*\*age, gender, and height.

Examination Survey (NHANES) III (1988-1994), MetS has a prevalence of 28.7% in overweight adolescents (BMI  $\geq$  95<sup>th</sup> percentile) when compared to at-risk adolescents (BMI  $\geq$  85<sup>th</sup> percentile to BMI  $<$  95<sup>th</sup> percentile), and 0.1% in children with normal weight (BMI  $<$  85) ( $P < 0.001$ ).<sup>9</sup>

Lee *et al.* studied the prevalence of MetS in a transversal study with 251 African-American and Caucasian children, using different definitions, and observed that MetS had a prevalence of 18.7%, according to the criteria of Weiss *et al.* (2004), 21%, according to the criteria of Cook *et al.* (2003), 13.4% using the criteria of Cruz *et al.* (2004, and 25.1%, according to Ford *et al.* (2005).<sup>25</sup>

Ferreira *et al.* investigated the prevalence of MetS and the risk factors for CVD in obese Brazilian children. The authors observed a prevalence of 17.3%, in obese children, and several risk factors for CVD, which showed a strong correlation with IR measured by Homeostasis Model Assessment – Insulin Resistance (HOMA-IR).<sup>23</sup> In another Brazilian study in São Paulo with school children aged 6 to 10 years, the authors observed that overweight and obesity were associated with MetS, with a prevalence of 25.8% (ATP III– Adult Treatment Panel – criteria) and 5.2% (WHO – World Health Organization – criteria), respectively, in overweight children, and 9.3% and 1.9%, respectively, in children with normal weight.<sup>4</sup>

Studies evaluating the prevalence of metabolic syndrome in JIA were not found.

Due to the difficulty to interpret prevalence studies on MetS because of the use of different criteria, a review of the literature on the prevalence of each specific component of the syndrome would be interesting. Therefore, one would have a better idea on the extension of this health problem in childhood and JIA.

## COMPONENTS OF THE METABOLIC SYNDROME

### 1) Childhood obesity

Childhood obesity is a public health concern, and it is directly related to the risk of developing complications of MetS.<sup>2</sup>

The presence of at least one risk factor for CVD (hypertension, dyslipidemia, or hyperinsulinemia) has been observed in 60% of overweight children and adolescents, while 20% have two or more risk factors. Besides those risks, obese children are at a higher risk of remaining obese in adult life, and 70% of them become obese adults.<sup>26</sup>

In a longitudinal study with 191 obese adolescents, Srinivasan *et al.* observed that 58% became obese adults, with an incidence of hypertension 8.5 times higher and levels of low-density lipoprotein (LDL-c) and TG 3.1 and 8.3 times greater, respectively, when compared to those that were not overweight in adolescence.<sup>27</sup>

The prevalence of obesity in American children and adolescents is approximately 20%.<sup>28</sup> In European countries,

the prevalence of overweight and obesity among children 7 to 11 years is to 30% and adolescents between 13 and 17 years the prevalence varies 20-35%.<sup>29</sup>

In Brazil, a study in public and private schools in Bahia were observed a prevalence of 9.3% of overweight and 4.4% obesity in children. The prevalence in public schools was 6.5% and 2.7%, respectively, and in private schools, it was 13.4% and 7.0%, respectively.<sup>30</sup> In another study, in São Paulo, the prevalence of obesity, according to three anthropometric criteria – Cole, Must, and WHO, was 8.25%, 16.50%, and 11.73%, respectively, in eight public schools.<sup>31</sup> A recent population-based study in Santos, São Paulo, with 10,882 children between 7 to 10 years showed that overweight and obesity had a prevalence of 15.7% and 18%, respectively.<sup>32</sup> The study of Strufaldi *et al.* showed a prevalence of 14.4% and 13.3%, respectively.<sup>4</sup>

It is known that obesity is a common complication of chronic inflammatory diseases in children and adults, probably reflecting the lack of activity imposed by the disease and treatment with glucocorticoids.<sup>33</sup> In a German study with 2778 JIA patients, the authors observed a prevalence of 15% of overweight and 5% of obesity. The prevalence of overweight was higher in patients on higher doses of corticosteroids ( $P < 0.04$ ), but this association was not maintained after logistic regression analysis.<sup>34</sup>

In study with 116 JIA patients, was observed a prevalence of overweight in 23.3% of the patients, and excess adiposity, according to measurements of the tricipital skin-fold, in 12.1% of the patients. In this population, we did not identify a significant association between obesity and the use of glucocorticoids (data not shown).<sup>18</sup>

## 2) Abdominal obesity

The distribution of body fat, specifically visceral fat, seems to be the link between the adipose tissue and IR, a characteristic of the MetS.<sup>35</sup>

Body fat distribution can be evaluated by a variety of anthropometric procedures. The waist-hip ratio (WHR) has been used in adults.<sup>36</sup> However, several studies have demonstrated that waist circumference (WC) can be a more reliable tool to determine abdominal obesity, including children.<sup>37</sup>

Studies with children have shown a good correlation between WC and IR,<sup>37</sup> and that WC can identify the risk of a child to develop metabolic and cardiovascular complications.<sup>38,39</sup>

Hirschler *et al.*, investigated the association of WC and MetS in children, and observed prevalences of increased

waist circumference (percentile  $\geq 90^{\text{th}}$ ) of 0%, 28.6%, and 86.5% in children with normal weight, overweight, and obesity, respectively. The authors concluded that, in children and adolescents, WC is a predictor for MetS and it should be included in clinical practice to identify the risk of cardiovascular diseases in children.<sup>38</sup>

In another Brazilian study, the authors investigated the frequency of MetS in 59 overweight and obese children in the outpatient clinic of a university hospital in São Paulo, observing that WC was increased in 88.1% of the patients (percentile  $\geq 90$ ).<sup>24</sup>

In patients with JIA, we found no studies about abdominal obesity.

## 3) Insulin resistance

Insulin resistance and elevated fasting plasma insulin levels, which are very common in obese individuals, seem to be the first sign for the development of T2DM.<sup>33,40,41</sup> Although the HOMA-IR, one of the methods used more often to estimate IR, is well established for epidemiological studies, a consensus on the use of this tool in clinical practice, with the possibility of anticipating preventive measures, does not exist.<sup>42</sup>

Several studies have suggested that overweight and obesity in children and adolescents are associated with IR and the development of T2DM. In American adolescents, according to NHANES III, T2DM has a prevalence of 4.1 in 1,000 individuals, which is higher than the prevalence of type 1 diabetes mellitus (1.7 in 1,000).<sup>2</sup>

A study with 55 obese children and 112 obese adolescents demonstrated a reduction in glucose tolerance of 25% and 21%, respectively, and 4% of the adolescents also had T2DM. The HOMA-IR was a strong predictor for the reduction in glucose tolerance, confirming that IR in childhood, associated with hyperinsulinemia, is an important risk factor for the reduction of glucose tolerance in children.<sup>40</sup>

Thorsdottir *et al.* investigated the association between anthropometric measurements and insulin concentration in 262 children and adolescents aged 9 to 15 years. They observed a positive correlation between obesity and insulin levels, but 14 to 20% of the children had normal weight and elevated insulin levels. These children have risk of weight gain when compared to children with normal weight and insulin levels.<sup>44</sup>

In another study, the authors investigated the distribution of insulin and IR, assessed by the HOMA-IR index, in adolescents between 12 and 19 years of age. The HOMA-IR index of girls was higher than that of boys. Obese children ( $\text{BMI} \geq 95^{\text{th}}$  percentile) had elevated HOMA-IR index when compared to

children with normal weight (BMI  $\geq$  85<sup>th</sup> percentile). Insulin resistance had a prevalence of 52.1%.<sup>41</sup>

We found no studies in the literature evaluating the prevalence of insulin resistance in JIA patients.

#### 4) Dyslipidemia

Risk factors for CVD, especially the lipid profile, have been investigated in children and adults with rheumatic diseases.<sup>45</sup>

Lipid abnormalities, especially hypertriglyceridemia and low HDL-c, show a strong association with IR.<sup>46</sup>

The prevalence of dyslipidemia in children and adolescents ranges from 2.9 to 33% considering total cholesterol levels higher than 200 mg/dL.<sup>47</sup>

Maffeis *et al.* observed increased TG levels in 4% of girls and boys with normal weight, and obesity in 26.2% and 17.6%, respectively. Zamboni *et al.* observed a prevalence of 15% of hypertriglyceridemia, 33% of hypercholesterolemia, and 52% of low HDL-c in obese children and adolescents.<sup>48</sup>

Urban *et al.* (2004) investigated serum lipid levels (total cholesterol, LDL-c, HDL-c, and TG), homocysteine, and CRP in 25 children with JIA and 15 healthy children. The authors observed a significant increase in TC, LDL-c, and TG, and reduction in HDL-c in JIA patients. Homocysteine showed a significant correlation with total cholesterol and LDL-c levels.<sup>49</sup> In another study with JIA patients, the authors evaluated plasma lipoproteins and observed a marked increase in TG and very low-density lipoprotein (VLDL-c) levels and significant reduction in HDL-c levels. Dyslipoproteinemia was observed in patients with higher disease activity, and longer disease duration seemed to increase the risks of atherosclerosis.<sup>50</sup>

#### 5) Hypertension

Childhood hypertension is associated with obesity and is the most important risk factor for the development of CVD in children.<sup>51</sup> The association of cardiovascular risk factors, including overweight, IR, and dyslipidemia, is increasingly more common in hypertensive children.<sup>52</sup>

Hypertension in childhood is defined by a systolic or diastolic blood pressure  $\geq$  95<sup>th</sup> percentile adjusted for gender, age, and height.<sup>53,54</sup> The prevalence of hypertension in children and adolescents is not negligible. It varies widely in different reports national and foreign authors, from 1% to 13%, according to the methodology used.<sup>55</sup>

The presence of hypertension in younger individuals in the United States has increased over the last few years. In a study with 1,740 American students, Jago *et al.* observed a 24% prevalence of some type of pressure change: increase in

systolic or diastolic pressure, or pre-hypertension, which is elevated when compared to the prevalence of 8% reported in the NHANES study.<sup>57</sup>

Moura *et al.* investigated the prevalence of hypertension in Brazilian children. They observed elevated blood pressure in 28.6% of overweight children, which is significantly different than in children with normal weight (8.1%,  $P < 0.0001$ ) and in children at-high risk for obesity (12.1%,  $P = 0.016$ ). Evaluation of the nutritional status by the BMI identified overweight and obesity in 9.3% and 4.5%, of the children, respectively.<sup>58</sup> In another study with Italian children, the authors reported a 1% prevalence of hypertension in girls and 1.9% in boys with normal weight, and 52.5% and 62.7% in overweight or obese children, respectively.<sup>39</sup>

Due to the absence of studies on hypertension in JIA patients, the prevalence of this disorder in Brazil is not known.

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## RISK FACTORS FOR METABOLIC SYNDROME

### 1) Glucocorticoids

Glucocorticoids are routinely used as anti-inflammatories and in immunosuppressive therapies.<sup>17</sup> They can be used systemically by different routes of administration, different doses, and different duration. Glucocorticoids affect several types of cells involved in the inflammatory process. Those drugs also inhibit several pro-inflammatory responses of endothelial cells.<sup>59</sup>

The side effects of corticoids, such as delayed growth, hypertension, T2DM, and obesity, as well as the fact that several of them are also independent risk factors for CVD, are well known.<sup>60</sup> However, some studies have reported that, due to the anti-inflammatory and anti-proliferative actions, corticotherapy can be cardio-protective.<sup>61</sup> Wei *et al.* investigated the association of corticotherapy and cardiovascular risk factors in 68,781 patients treated with glucocorticoids and 82,202 patients not treated with those drugs, hospitalized between 1993 and 1996. The authors observed that the risk of cardiovascular disease, including myocardial infarction and stroke, was higher in patients treated with more than 7.5 mg/day of prednisolone for one to five years.<sup>17</sup>

Our group investigated the impact of the inflammatory activity and use of glucocorticoids in nutritional parameters of patients with JIA. We observed that the cumulative dose of glucocorticoids was not independently associated with short stature or other nutritional parameters.<sup>18</sup> Longitudinal follow-up for one year showed that the growth rate had a significant association with serum levels of IL-6, but not with

the cumulative dose of glucocorticoids. Those observations indicate a more predominant role of inflammatory mediators on growth than the chronic exposure to glucocorticoids. The question of whether the same is true for MetS and cardiovascular risk is yet to be determined.

## 2) Inflammation

Metabolic syndrome and obesity are considered diseases associated with chronic inflammation. Inflammation is a known component of atherosclerosis, and, recently, some components of MetS have been related to inflammatory markers.<sup>63</sup>

This inflammatory process can be identified by elevated levels of IL-6, TNF $\alpha$ , and CRP. Presumably, TNF $\alpha$  and IL-6 work as inflammatory mediators in metabolic disorders, and, in children, they are associated with the degree of adiposity.<sup>54</sup> Most of those cytokines are directly or indirectly related to processes that contribute for atherosclerosis, hypertension, IR, T2DM, and dyslipidemia, *i.e.*, they could represent a link among adiposity, MetS, and CVD.<sup>64</sup>

C-reactive protein is a marker of inflammatory processes.<sup>65</sup> Serum levels of CRP are highly sensitive and show a direct relationship with the degree of childhood obesity, and it could be a marker of atherosclerotic progression.<sup>54</sup>

The association of CRP with adipocytes, insulin, dyslipidemia, and hypertension has been shown in healthy pre-pubertal children.<sup>13</sup> In healthy adolescents, CRP was linked to IR and components of MetS.<sup>6</sup> Ford *et al.* investigated the association between MetS and CRP and observed that MetS was associated with elevated concentrations of CRP. Among patients with MetS, 38.4% had CRP levels > 3 mg/L, and 10.3% of patients without MetS showed the same levels ( $P < 0.007$ ).<sup>19</sup>

Studies showing a clear association between inflammatory activity and the development of MetS in children, but with JIA do not exist.

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## TREATMENT OF METABOLIC SYNDROME

Early detection of children and adolescents at risk for MetS is fundamental for fast intervention and risk reduction. Several factors are involved in the genesis of MetS, and, for this reason, several measures should be taken to prevent it.

The prevention and treatment of MetS should be based on lifestyle changes, with emphasis on dietary reeducation and regular physical activities. Dietary intervention is aimed at reducing the ingestion of calories, fats, simple sugars, and sodium and increasing the intake of fiber. Treatment objectives include normalization of blood glucose levels, blood pressure,

serum lipid levels, and body weight.<sup>53,54</sup> Pharmacologic treatment is reserved for patients with a diagnosis of diabetes.<sup>54</sup>

Weight loss has higher impact on MetS. Data in the literature show that a weight loss of 7% to 10% is capable of reducing waist circumference, lipid profile, and blood glucose levels.<sup>66</sup> Treatment of childhood obesity is paramount, and involving the child and adolescent, their families, and their social environment are fundamental to stimulate lifestyle changes.<sup>67</sup>

It is increasingly more clear the need of preventive strategies to reduce the risk of CVD in adult patients with rheumatic diseases. Adult rheumatic diseases, such as rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE), have higher morbidity and mortality rates from early CVD due to the chronic inflammatory overload and reduction in physical activities. Recent data indicate that suppression of inflammation reduces morbidity and mortality rates of CVD in patients with severe RA. Those strategies should be based on understanding the role of inflammation in CVD, as well as management of risk-related lifestyles. Suppression of inflammation by treating RA patients with powerful antirheumatic drugs, as well as TNF inhibitors, can reduce the risk of cardiovascular events.<sup>68</sup> Other prevention strategies include regular laboratorial exams, to intervene in traditional risk factors, and treatment of dyslipidemia, hypertension and DM, besides stimulating smoking cessation and maintenance of a regular activity program.<sup>68,69</sup>

Currently, studies evaluating the specific treatment of this set of risk factors in children with JIA are not available. Regardless of disease subtype, we suggest that adequate control of the inflammatory response, similar to that used in adult patients, and the use of available treatment resources, such as reducing obesity, increasing physical activities, and measuring and treating different components of MetS, should be done.

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## CONCLUSION

The prevalence of metabolic syndrome is increasing among children and adolescents. However, there is no uniformity between the parameters for the diagnosis of the metabolic syndrome in pediatric population, hindering comparison among different populations. The development of metabolic syndrome is associated with the increased risk of T2DM and cardiovascular diseases. Early diagnosis of children and adolescents at risk for metabolic syndrome is crucial for fast intervention and risk reduction. In JIA, there are no studies evaluating the prevalence of metabolic syndrome. Current data indicates a higher prevalence of obesity and dyslipidemia. The interactions among components of the metabolic syndrome, inflammation,

use of glucocorticoids, and other treatments has been actively explored in inflammatory arthropathies and systemic lupus erythematosus in adults, indicating an extremely complex situation. This scenery cannot be extrapolated directly to children and adolescents with JIA, and specific studies in this population are required to identify effective strategies for the prevention and adequate management of metabolic and cardiovascular complications in those patients.

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