

RESEARCH ARTICLE

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SCIENTIFIC EVIDENCE ABOUT THE ASSOCIATION BETWEEN THE METABOLIC SYNDROME (MS) WITH NUTRITIONAL STATE AND SEXUAL MATURATION STAGE

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ABSTRACT

During puberty, anthropometric changes and body composition of adolescents occur, with an impact on nutritional status, increasing the risk of cardiovascular diseases resulting from excess body fat. The aim of this study was to identify scientific evidence that demonstrates the association between metabolic syndrome (MS), sexual maturation stage and nutritional status in adolescents. This is an integrative review of the literature carried out at SciELO and PubMed, without a time frame, with the following guiding question: *What scientific evidence demonstrates the association between metabolic syndrome (MS), with the stage of sexual maturation and nutritional status?* The results showed 16 articles, grouped by similarity and according to the categories: Sexual Maturation versus Metabolic Syndrome, Sexual Maturation versus Nutritional Status and Nutritional Status versus Metabolic Syndrome. The findings showed that the prevalence of MS increases with the presence of obesity, and that early sexual maturation was positively associated with obesity in adolescents; moreover, in girls, early menarche was associated with childhood obesity. There is a need to establish a criterion for MS, since there was an absence of well criteria and reference established values for MS among children and adolescents, making comparisons of prevalence difficult.

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INTRODUCTION

Adolescence is a period of physical and psychic changes, marked by an intense process of biopsychosocial growth and development. These changes are influenced by endogenous and exogenous factors (MIRANDA, ORNELAS & WICHI, 2011; MIRANDA, by FARIA & PRIORE). In view of the increasing prevalence of obesity observed in all stages of life, it is estimated that isolated metabolic abnormalities and Metabolic Syndrome (MS) are also increasingly common among children and adolescents (STEINBERGER *et al.*, 2009). According to the *International Diabetes Federation* (IDF, 2007) for adolescents from 10 to 16 years of age, MS is a combination of abdominal obesity, a mandatory criterion for diagnosis, and two or more clinical characteristics (triglycerides, HDL-cholesterol, blood

pressure systolic / diastolic blood pressure, fasting glucose) included in this definition (ALBERTI & ZIMMET, 2006). The presence of MS increases the risk of developing cardiovascular diseases and other pathologies resulting from excess body fat (ALBERTI & ZIMMET, 2006;). It is known that during puberty the changes that occur cause anthropometric changes and body composition of adolescents with an impact on nutritional status. In recent years, the frequency of obesity among Brazilian adolescents has increased, representing almost double, from 4.9% (IBGE, 2010) to 8.4% (BLOCH *et al.*, 2016). In this scenario, it is known that about 70% of obese adolescents become obese adults and, consequently, will be at high risk of developing cardiovascular diseases and other pathologies resulting from excess body fat (ALBERTI & ZIMMET, 2006). To assess the nutritional status of individuals, the body mass index (BMI) is

widely used, due to its low cost when compared to other methods. The different criteria for the nutritional classification of adolescents are based on BMI reference values according to age and gender, however, it is not associated with the stage of sexual maturation that best characterizes the stage of development of this population. The stage of sexual maturation influences the distribution of body fat, causing metabolic disorders. These changes during puberty cause anthropometric and body composition changes in adolescents with an impact on nutritional status. There is a tendency towards a greater accumulation of fat among girls and an increase in muscle mass in boys, due to the actions of the hormones estradiol and testosterone, respectively (FRIGNANI *et al.*, 2015). Pubertal development follows a physiological chronology of events due to changes in the pattern of secretion of some hormones. The activation of the hypothalamic-pituitary-gonadal axis triggers, under gonadotropin stimulation, the secretion of sexual steroids (predominantly testosterone in boys and estradiol in girls) that are responsible for the morphological changes of the pubertal period. The production of these hormones results in the appearance of secondary sexual characters marking the beginning of puberty (SIEVORGEL *et al.*, 2003). The present study aimed at identifying scientific evidence that demonstrates the association between MS considering the stage of sexual maturation and nutritional status in adolescents.

MATERIALS AND METHODS

A study of the type of integrative literature review was proposed, carried out with search in journals, without time limitation, since there was a scarcity of studies relating MS with the degree of sexual maturation of adolescents. We opted for this methodology, in view of being a tool capable of carrying out a systematic survey of the literature, demonstrating the state of the art of scientific publications.

presentation of the integrative review. The formulation and identification of the research problem was defined with the research problem raised, and the guiding question was: "What scientific evidence demonstrates the association between metabolic syndrome (MS), with the stage of sexual maturation and nutritional status?" The descriptors were first identified with the database of the Virtual Health Library (Health Sciences Descriptors - DeCs - <http://decs.bvs.br/>) and Pubmed [National Library of Medicine National Institutes of Health, United States of America (USA)], Scielo [Scientific Electronic Library Online] and Lilacs [Latin American and Caribbean Literature in Health Sciences] namely: *Sexual Maturation, metabolic syndrome, and nutritional status*. These keywords were combined using AND or OR, and searched only for the English vernacular. As established criteria, the following were included: scientific and/ or observational research articles published in the established period, available in full in electronic format, in Portuguese, Spanish or English. The time frame has not been established. Exclusion criteria: absence or incompleteness of articles available in the databases, clinical trials on animals, course conclusion paper, dissertations and doctoral thesis. For the systematization of the data, the extracted articles went through an exploratory reading and later file of the selected texts. For data analysis, it was based on a critical analysis of the all the studies, which were carefully read, allowing the construction of the "study corpus" to contribute to the discussion of the results. This analysis was performed through the interpretation of the studies and types of studies. After this stage, the findings were categorized by similarity, and presented in a descriptive table. The study meets the guidelines and regulatory standards for research involving human beings, defined by the Resolution of the National Health Council and dispenses with the need for submission to the Research Ethics Committee.

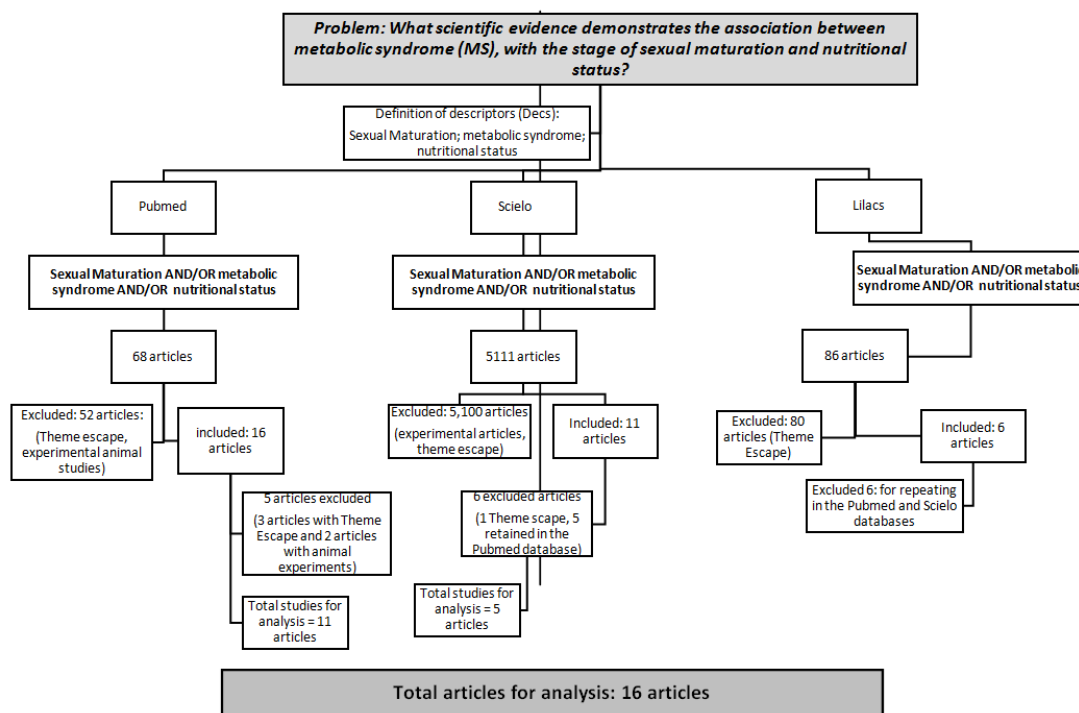


Figure 1. Flowchart of the steps for selecting articles for analysis

According to Souza, Silva and Carvalho (2010), the integrative review permeates by important stages, among them: 1) Formulation and identification of the research problem; 2) searching or sampling in the literature; 3) data collection; 4) critical analysis of the included studies; 5) discussion of results; 6)

RESULTS

5,254 articles were found on nutritional status, metabolic disorders and sexual maturity. After applying the inclusion and exclusion criteria, 16 articles were selected for this analysis.

Chart 1. Corpus of analysis of the integrative review, according to studies published between 2002 and 2020 (N = 16)

C	Title	Data base	Objective	Kind of study
Sexual maturation versus nutritional status	Influence of obesity on timing of puberty[Biro, Khoury e Morrison, 2006]	Pubmed	Discussing the relationship between obesity and the time of puberty and the factors that contribute to secular changes in obesity	Narrative Literature Review
	Timing and secular trend of pubertal development in Beijing girls [Chen, Wang e Mi, 2014]		Identifying the timing of pubertal characteristics and the age-old trend of menarche among girls in Beijing, from the 1980s to the 2000s	Retrospective cohort, with 9778 girls aged 6 to 18 years old [China]
	Pubertal timing and adult obesity and cardiometabolic risk in women and men: a systematic review and meta-analysis [Prentice e Viner 2012]		Analyzing the association between pubertal time and adult obesity is likely to be confused by childhood adiposity	Systematic review
	Association between obesity and sexual maturation in Chinese children: a multicenter study [Dai et al., 2014]		Assessing the current status of sexual maturation in Chinese children, examine the association between obesity and early sexual maturation in boys and compare it with girls and test the hypothesis that the associations differ by gender	Cross-sectional study with 9812 boys and 8895 girls aged 6 to 18 years. [China]
	Ethnic and sex differences in body fat and visceral and subcutaneous adiposity in children and adolescents [Staiano e Katzmarzyk, 2012]		Examining the variation in pediatric total body fat (TBF), visceral AT (IVA) and subcutaneous AT (SAT) due to age, gender, maturation status and ethnicity	Systematic review
	Timing of Pubertal Milestones in Low- and Middle-Income Countries: A Systematic Review and Meta-Analysis [Mododie et al., 2020]		Determining the age of menarche (AAM) and the age of onset of puberty [breast Tanner stage female 2 (B2) and male Tanner stage genital 2 (G2)] among healthy adolescents living in low and middle income countries, and exploring the impact of nutritional status in pubertal time in this population	Systematic review
	Influência dos estágios de maturação sexual no estado nutricional, antropometria e composição corporal de adolescentes [Barbosa, Franceschini, e Priore, 2006].	SciELO	Analyzing the influence of sexual maturation stages in the state nutritional status, anthropometry and body composition of adolescents of both genders	Narrative literature review
	Nutritional status and pubertal stage of adolescents from one public school and one private school from Rio de Janeiro, Brazil [Oliveira e Veiga, 2005]	SciELO	Assessing the nutritional status and sexual maturation of adolescents aged 11 to 15.9 years, from different socioeconomic levels	Cross-sectional study with 502 adolescents of both genders, from 11 to 15.9 years [Brazil]
	Influence of sexual maturation on body mass index of Low Socioeconomic level adolescents of Rio De Janeiro [Coelho, Sichieri e González, 2002]	SciELO	Verifying the importance of sexual maturation in nutritional assessment based on body mass index (BMI)	Cross-sectional study [Brazil]
Sexual Maturation versus Metabolic Syndrome	Public Health Implications of Altered Puberty Timing [Golub et al., 2008]	Pubmed	Discussing the implications of secular trends at the time of puberty: first, at the individual level in clinical pediatrics; second, at the population level, with regard to the consequences for adult health; and, third, child health risk assessment of environmental chemicals.	Systematic review
	Association between dyslipidemia and anthropometric indicators in adolescents [Lima et al., 2011]	SciELO	Investigating the association between dyslipidemia and other risk factors for cardiovascular disease (CVD) in adolescents, considering sexual maturation	Cross-sectional study with 432 adolescents [Brazil]
Estado nutricional versus Síndrome Metabólica	Dietary factors associated with metabolic syndrome and its components in overweight and obese Brazilian schoolchildren: a cross-sectional study [Rinaldi et al., 2016]	Pubmed	Exploring MS and its components according to anthropometric and demographic factors and evaluating the relationship between the components of MS and the characteristics of the diet in overweight and obese students.	Cross-sectional study with 147 students (6 to 10 years old) [Brazil]
	Metabolic syndrome in obese adolescents: what is enough? [Sewaybricker et al., 2013]		Studying the agreement between three different criteria for metabolic syndrome (MS) adapted to adolescents and identifying factors associated with MS.	Cross-sectional study with 65 obese 10 to 18 years old [Brazil]
	The relationship between body composition and selected metabolic syndrome markers in black adolescents in South Africa: The PLAY study [Zeelie, Moss e Kruger, 2010]		Determining the relationship between body composition and selected metabolic syndrome markers in black adolescents.	Cross-sectional study with 232 adolescent boys and girls aged 15 to 19, [South Africa]
	Longitudinal preventive-screening cutoffs for metabolic syndrome in adolescents [Flouris et al., 2008]		Detecting metabolic cut-off points for risk factors in adolescence for the diagnosis of metabolic syndrome that develops at age 17	Prospective cohort with adolescents aged 12 to 17 [Greece]
	Prevalência de Síndrome Metabólica e associação com estado nutricional [Mendes et al., 2019]	SciELO	Determining the prevalence of metabolic syndrome and verifying its association with nutritional status in adolescents.	Cross-sectional study with adolescents between 14 and 19 years old. [Brazil]

The selection steps, according to the three databases, are presented in the flowchart. The selected articles were categorized according to their similarity, with three categories being created: Sexual Maturation *versus* Metabolic Syndrome, Sexual Maturation *versus* Nutritional Status and Nutritional Status *versus* Metabolic Syndrome. A *corpus* of data analysis was prepared to present the articles selected for discussion, being presented through Table 1.

DISCUSSION

The articles found were published between 2002 and January 2020, based on research conducted in the United States of America, China, Greece, Brazil and South Africa. Of the 16 articles analyzed, nine discussed the relationship between obesity and the time of puberty, analyzing the influence of sexual maturation stages on the body composition of adolescents of both genders (BIRO, KHOURY and MORRISON, 2005; CHEN, WANG and MI, 2014; PRENTICE and VINER 2013; DAI *et al.*, 2014; STAIANO and KATZMARZYK, 2012; MODODIE *et al.*, 2020; BARBOSA, FRANCESCHINI, and PRIORE, 2006; OLIVEIRA and VEIGA, 2005; COELHO, SICHIERI and GONZÁLEZ, 2002). Of these nine, sexual maturation was correlated with nutritional status, five of them underwent a systematic review, where they observed that excess weight is present in the more advanced stages of sexual maturation, with girls experiencing a gradual increase in body fat stocks and, among boys, fat loss and muscle mass increase may occur in the late adolescence phase (BIRO, KHOURY and MORRISON, 2005; STAIANO and KATZMARZYK, 2012; MODODIE *et al.*, 2020; BARBOSA, FRANCESCHINI, and PRIORE, 2006; PRENTICE and VINER 2013).

Of the five systematic review articles, three of them discuss early puberty development that may be influenced by the increase in the Body Mass Index (BMI), with the interaction of genetic, racial, environmental factors and in the higher social classes (BIRO, KHOURY and MORRISON, 2005; STAIANO and KATZMARZYK, 2012; MODODIE *et al.*, 2020). Of the nine that discuss sexual maturation influenced by nutritional status, four developed a cross-sectional study (DAI *et al.*, 2014; OLIVEIRA and VEIGA, 2005; COELHO, SICHIERI and GONZÁLEZ, 2002), of which four, one was a retrospective cohort (Chen, Wang and Mi, (2014)). This cohort study carried out in China by Chen *et al.* (2014), evaluated girls aged 6 to 18 years in the urban and rural areas to identify the pubertal characteristics and the period of menarche. They concluded that the urban girls' menarche decreased by 4.2 months / decade and rural girls from 9.6 months / decade from 1980 to 2004. In other words, urban girls mature earlier than rural girls in Beijing, with a secular tendency to decline of menarche markedly in rural areas. And the other three studies concluded that obesity is positively associated with sexual maturation in boys and girls, and the association does not differ by gender, showing the importance of sexual maturation in the evaluation by BMI (DAI *et al.*, 2014; OLIVEIRA and VEIGA, 2005; COELHO, SICHIERI and GONZÁLEZ, 2002).

Of the sixteen articles analyzed, two discuss premature sexual maturation with a risk factor for the onset of metabolic syndrome, analyzing the influence of sexual maturation stages on the body composition of adolescents. Golub *et al.* (2008), in a systematic review, clearly discuss premature menarche, influenced by environmental factors, as a risk factor for the onset of metabolic syndrome in adults, demonstrating the importance of discovering the mechanisms at the time of puberty and the reasons for its changes, this will provide tools to improve children's health risk assessment early. Lima *et al.* (2011) conducted a cross-sectional study in adolescents investigating the association between

dyslipidemia and other risk factors for cardiovascular diseases, with high density lipoprotein (HDL-C) being the most prevalent dyslipidemia, and the most prevalent hypertriglyceridemia in adolescents with excess of weight. However, they found no association between sexual maturation and concentrations of total cholesterol and low-density lipoprotein (LDL-C), regardless of age and BMI, justifying that concentrations of lipids and lipoproteins change during growth and development, showing two phases of life of expressive increase: up to 2 years and during pubertal development. In this study, sexual maturation was considered as a control variable, they found no influence on the HDL-C ratio, probably due to the age of the adolescents. However, HDL-C was the most prevalent dyslipidemia in this finding, and the combination with hypertriglyceridemia is important in the pathogenesis of the metabolic syndrome. Of the sixteen articles analyzed, five discuss metabolic syndrome associated with nutritional status, they observed that the prevalence of MS increased directly with the degree of obesity (MENDES *et al.*, 2019; RINALDI *et al.*, 2016; SEWAYBRICKER *et al.*, 2013; ZEELIE, MOSS, KRUGER, 2010; FLOURIS *et al.*, 2008). One of these articles studied the agreement between three different criteria for MS adapted for adolescents. Sewaybricker *et al.* (2013) conducted a cross-sectional study with obese adolescents. MS was defined using the criteria of the World Health Organization (WHO), presented in 1998 with an emphasis on risk factors for type 2 diabetes. In 2001, the Adult Treatment Panel III (ATP III), presented a definition focused on diseases cardiovascular diseases, and in 2007 the International Diabetes Federation (IDF) developed a criterion aimed at children from 10 years onwards. They concluded that WHO criteria do not seem to be suitable for adolescents. The IDF and ATP III criteria had an excellent agreement. Puberty and triglycerides have been associated with MS. Increased body fat, especially visceral fat, has been associated with the development of chronic diseases in adults. Due to the increase in obesity among children and adolescents and the risk factors for cardiovascular diseases, interest in investigating the presence of metabolic changes similar to those observed in adult MS has emerged.

Conclusion

The findings of the present review show the difficulty of relating criteria and reference values of MS for children and adolescents, as it was observed that there is no consensus on the best definition of this syndrome, as there are still differences between the components and the cut-off points, which can make it difficult to compare the prevalences reported in different studies. In addition, another difficulty involves the question of the physiological influence of puberty, as it is a phase characterized by a period of transition, with accelerated changes in the metabolic system such as hormonal regulation, changes in body fat and its distribution, strongly influenced by sexual maturation, showing that in adolescence, to assess nutritional status, as well as changes in body composition, one should consider not only the chronological age, but also the stage of sexual maturation. Some strengths were observed in the articles analyzed, where the prevalence of MS directly increased with the degree of obesity, that premature menarche, influenced by environmental factors, can be a risk factor for the onset of the metabolic syndrome in adults, that the excess of weight is present in the most advanced stages of sexual maturation and that there are no well-established criteria and reference values for MS among children and adolescents, making comparisons of prevalence difficult. Considering the relevance of the theme, it is important to know the dimension of this problem by investigating studies that demonstrate metabolic changes in children and adolescents, as well as the evolution of the criteria used for its classification.

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