

Obese girls face heightened risk of cardiovascular disease in adulthood

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A study of 92 adolescents conducted in Brazil suggests girls are more likely than boys to develop metabolic alterations associated with obesity, such as high blood pressure and excessive blood levels of cholesterol and triglycerides (dyslipidemia).

The study was conducted with FAPESP's support by scientists affiliated with the University of São Paulo's Biomedical Sciences Institute (ICB-USP) and the Medical School of Santa Casa de Misericórdia de São Paulo (FCM-SCMSP). The findings are reported in an article in the journal *Frontiers in Nutrition*.

According to the authors, the obese girls displayed a pattern of lipid profile alterations not seen in girls without obesity and a higher propensity to develop cardiovascular disease in adulthood. "We found that girls have a much greater tendency to undergo the alterations typical of obesity, such as elevated blood pressure and dyslipidemia. In our study, they had augmented levels of triglycerides and LDL, so-called 'bad cholesterol,' while HDL, 'good cholesterol,' was lower than in eutrophic [\[normal weight\]](#) girls," said Estefania Simoes, first author of

the article.

The lipid profile of the obese boys included in the study displayed no significant differences from that of normal-weight boys, according to the researchers.

Childhood obesity is a growing concern among health authorities and scientists in the field. The World Health Organization (WHO) estimates that some 340 million children aged 5-19 worldwide were overweight or obese in 2016. It is well known that childhood obesity is associated with a higher likelihood of metabolic disorders and cardiovascular disease in adulthood.

A substantial amount of research shows this, but the differences between boys and girls in terms of the effects of obesity have not been studied in depth. "We compared obese and non-obese girls and boys aged 11-18, simultaneously addressing anthropometrics, lipid and lipoprotein profile, and hormone and neuropeptide levels, with a special emphasis on sex-dependent responses. To our knowledge, this is the first study to take this multifactor approach," Simoes said.

The study was funded by FAPESP via two projects: "Cerebral anatomy, [inflammatory mediators](#) and appetite regulatory hormones in obese pediatric patients: A neurobiological study of obesity" and "Systemic inflammation in cachectic cancer patients: Mechanisms and therapeutic strategies, a translational medicine approach."

Collaborations

The study was conducted in collaboration with Ricardo Riyoyti Uchida, a neurologist and psychiatrist who acted as principal investigator and recruited the 92 participants at the Child Obesity Outpatient Clinic of the Santa Casa de Misericórdia Hospital in São Paulo. Uchida uses neuroimaging to try to find out whether there are alterations in the

brain regions associated with satiety and appetite in obese subjects. "An article on this topic is about to be published, focusing on characterization of the central nervous system in obese patients. Uchida has been studying adolescent obesity for many years," Simoes said.

The SCMSp team took the subjects' blood pressure and collected blood samples to measure fasting serum concentration of total cholesterol (TC), high-density lipoprotein cholesterol (HDL), low-density lipoprotein cholesterol (LDL), very-low-density lipoprotein cholesterol (VLDL), and triglycerides (TG).

The researchers also looked for binge eating patterns and addiction to high-sugar and high-fat foods using special-purpose questionnaires. They also measured neuropeptides linked to neuro-humoral alterations and detected significant alterations in obese subjects. Neuropeptides are released in response to peripheral signals such as hormones to regulate appetite and energy balance. "In addition, leptin and insulin interact with neuropeptides NPY, MCH and α -MSH, not only regulating appetite but also activating the sympathetic nervous system, which may contribute to the [high blood pressure](#) associated with obesity," Simoes said.

The new data on differences between girls' and boys' hormone, cytokine and neuropeptide profiles points to the need for personalized treatment. "However much we may want to design a single therapeutic strategy based on drugs or food supplements, our findings show that girls and boys shouldn't be treated alike even if they have the same weight and age, because their organisms respond to treatment differently," Simoes said.

Fruitful research

According to Joanna Correia-Lima, second author of the article, two other papers were written using the data collected from the same group of volunteers. The first, published in the *International Journal of Obesity*, focuses on characterizing the inflammatory process since systemic chronic inflammation is significant in obese subjects.

"At the laboratory headed by Professor Marília Seelaender, a co-author with us of both articles, we've long been studying a disorder that's the opposite of obesity: cachexia [extreme weight loss and muscle wasting, frequently in cancer and AIDS patients]. Systemic inflammation plays a key role in both," Correia-Lima said. "We first focused on inflammation and then on the role of hormones and how they relate to the predisposition to develop cardiovascular disease."

Most scientific publications on childhood obesity, she added, focus on a single specific alteration, such as inflammation or a hormone, for example, or on a specific consequence of obesity such as high blood pressure. "Our research set out to connect the dots. We have a large cohort and a large amount of data, so we can characterize the links in this group, showing how all alterations in the obese organism are associated. The most important aspect of our work is showing these links," Correia-Lima said.

According to Simoes, it was the researchers' statistical analysis of the data that pointed to these links. "Elevated levels of hormones such as insulin and leptin [the satiety hormone] may be the cause of high blood pressure, for example," she said. "This kind of information should be taken into consideration when treating [obesity](#). Physicians often prescribe anti-inflammatory drugs, which can indeed mitigate one aspect of the disease, but the treatment will be more complete if you know about other contributing factors."

Obesity is a multifactor disease, and treatment cannot be one-size-fits-all. Diet and exercise are important, but medication may also be needed, as well as surgical intervention and psychotherapy. "Questionnaire-based assessments point to eating disorders at the psychological level among these girls and boys," Simoes said. "However much we show that there are alterations in neuropeptides and hormones, as well as high blood pressure, inflammation and so on, ultimately the child doesn't just have an organic problem but a psychological one. Hence the importance of [childhood obesity](#) studies, to assist early diagnosis and attempt timely treatment before adult complications set in."

More information: Estefania Simoes et al, Sex-Dependent Dyslipidemia and Neuro-Humoral Alterations Leading to Further Cardiovascular Risk in Juvenile Obesity, *Frontiers in Nutrition* (2021). DOI: [10.3389/fnut.2020.613301](https://doi.org/10.3389/fnut.2020.613301)

Estefania Simoes et al. Sex dimorphism in inflammatory response to obesity in childhood, *International Journal of Obesity* (2021). DOI: [10.1038/s41366-021-00753-1](https://doi.org/10.1038/s41366-021-00753-1)

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