Non-alcoholic fatty liver disease and metabolic syndrome in obese children

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Abstract

I read with great interest the article of Fu et al who investigated whether non-alcoholic fatty liver disease (NAFLD) is an early mediator for prediction of metabolic syndrome, and whether liver B-ultrasound could be used for its diagnosis, in a study involving 861 obese children (6-16 years old). In this study, it was reported that NAFLD is not only a liver disease, but also an early mediator that reflects metabolic disorder, and that liver B-ultrasound can be a useful tool for metabolic syndrome (MS) screening. The authors reported that NAFLD and MS were present in 68.18% and 25.67% of obese children, respectively. Moreover, they observed that the prevalence of MS in NAFLD children was 37.64%, which was much higher than that in the non-NAFLD group. Criteria analogous to those of the Adult Treatment Panel III definition for MS were used for children in this study. The reported prevalence data on MS in the young has varied markedly, in large part because of disagreement among the variously proposed definitions of MS. Therefore, in my opinion, a study aiming to assess the association between MS components and NAFLD in obese children has to take into account a simple, easy-to-apply clinical definition proposed by the international diabetes federation for MS. Interpretation of the results of the Fu et al study are limited by another major caveat: that the diagnosis or exclusion of NAFLD was based on liver enzymes and ultrasound imaging, but was not confirmed by liver biopsy. Indeed, it is known that liver enzymes may be within the reference interval in up to 70% of patients with diagnosed NAFLD and that the full histopathological spectrum of NAFLD may be present in patients with normal liver enzymes, which therefore cannot be reliably used to exclude the presence of NAFLD.

Key words: Non-alcoholic fatty liver disease; Metabolic syndrome; Obese children

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TO THE EDITOR

I read with great interest the article of Fu et al, who investigated whether non-alcoholic fatty liver disease (NAFLD) is an early mediator for prediction of metabolic syndrome, and whether liver B-ultrasound can be used for its diagnosis, in a study of 861 obese children (6-16 years old). In this study, it was reported that NAFLD is not only a liver disease, but also an early mediator that reflects metabolic disorder, and that
liver B-ultrasound can be a useful tool for metabolic syndrome (MS) screening. The authors reported that NAFLD and MS were present in 68.18% and 25.67% of obese children, respectively. Moreover, they observed that the prevalence of MS in NAFLD children was 37.64%, which was much higher than that in the non-NAFLD group. Criteria analogous to those of the adult treatment panel (ATP III) definition for MS were used for children in this study.

Since De Ferranti et al[3] demonstrated different prevalence rates of MS by using slightly different modifications of the ATP III criteria in the same population using the same dataset, there has been a need for standardization of MS in children. For example, De Ferranti et al[3] analyzed the same population which consisted of 2430 adolescents aged 12-19 years who had been previously evaluated by Cook et al[4] using slightly different criteria. Changing the criteria for the diagnosis increased the prevalence of the MS from 4.2% to 9.3% in the total population and from 28.7% to 31.2% among the obese population in the total cohort.

In our previous study[3], we have reported that MS defined according to modified WHO criteria adapted for children was found in 27.2% of young people, with a significantly higher rate among obese adolescents aged 12-18 years (37.6%) than among obese children aged 7-11 years (20%) (P < 0.001). Several studies have revealed race/ethnic differences in the prevalence of MS in children as well as in adults.

In 2007, recognizing how difficult it is to have multiple working definitions of the MS, the international diabetes federation (IDF) published its definition for children[8]. The new IDF definition is ranked according to age groups 6 to < 10 years, 10 to < 16 years, and ≥ 16 years. This was believed to be necessary because of the developmental challenges presented by age-related differences in children and adolescents. Children < 6 years were excluded as a result of insufficient data in this age group. The IDF suggests that below 10 year of age, the MS should not be diagnosed, and a strong message for weight reduction should be delivered to parents and caregivers of those with abdominal obesity.

As described, the reported prevalence data on MS in the young has varied markedly, in large part because of disagreement among the various proposed definitions of MS. Therefore, in my opinion, a study aiming to assess the association between MS components and NAFLD in obese children has to take into account the simple, easy-to-apply clinical definition proposed by the IDF for MS. Moreover, the statement: “There were significantly higher incidences concerning every component of MS in obese children with NAFLD compared with the non-NAFLD group” is unclear and probably wrong since data for MS were derived from a prepubertal age group most of whom were below 10 years of age. The major concern originates from the assumption that in order to validate such a result it is mandatory to consider a wide population of adolescents. The authors have not referenced other studies evaluating MS in children in this paper, but they offer a new observation.

Interpretation of the results of the Fu et al[1] study are limited by another major caveat that the diagnosis or exclusion of NAFLD was based on liver enzymes and ultrasound imaging, but was not confirmed by liver biopsy. Indeed, it is known that liver enzymes may be within the reference interval in up to 70% of patients with diagnosed NAFLD and that the full histopathological spectrum of NAFLD may be present in patients with normal liver enzymes, which therefore cannot be reliably used to exclude the presence of NAFLD[9]. Moreover, although liver ultrasonography is widely used for diagnosing NAFLD, this imaging method has good sensitivity and specificity only for detection of moderate and severe hepatic steatosis, but its sensitivity is reduced when hepatic fat infiltration on liver biopsy is < 33%[7]. Only liver biopsy can be used for diagnosing NAFLD and accurately determining the histological severity and prognosis of liver damage[9].

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