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Original Article

Prevalence, risk factors, and predictors of nonalcoholic fatty liver disease among schoolchildren: A hospital-based study in Alexandria, Egypt

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ABSTRACT

Background and study aims: Nonalcoholic fatty liver disease (NAFLD) is an emerging problem in children and adolescents worldwide. This study was done to investigate the prevalence of NAFLD in children and adolescents as well as to determine the associated risk factors of fatty liver and to explore the ability of some obesity indices to predict and consequently be used as a screening method of fatty liver disease at certain cutoff points in schoolchildren.

Patients and methods: A cross-sectional, nested case–control study was carried out. Cases and controls were randomly selected from outpatient schoolchildren aged 6–18 years attending the radiology clinic at Sporting Health Insurance Paediatric Hospital in Alexandria. They were subjected to ultrasonic examination as well as complete anthropometric and laboratory measurements including fasting plasma glucose (FPG) level, fasting insulin, alanine aminotransferase (ALT) level, and lipid profile.

Results: Fatty liver was prevalent in schoolchildren (15.8%) and increased significantly with age ($p = 0.004$). Positive family history of diabetes mellitus (DM), hypertension (HTN), obesity, and liver disease were all statistically significant risk factors for fatty liver. Waist circumference (WC), body mass index (BMI) and its *Z*-score were significantly sensitive predictors. BMI was considered the best predictor of paediatric NAFLD at a cutoff = 22.9. NAFLD was significantly associated with high triglycerides (TGs), low high-density lipoprotein cholesterol (HDL), homoeostatic model assessment (HOMA) percentile, and the number of metabolic syndrome (MS) components.

Conclusion: Paediatric NAFLD is a substantial problem in schoolchildren and has a close relationship with obesity, dyslipidaemia, insulin resistance (IR), and consequently MS. BMI and WC can be used as useful predictors and screening tools for NAFLD in schoolchildren.

Introduction

Nonalcoholic fatty liver disease (NAFLD) is the most common cause of chronic liver disease in developed countries and presents an emerging problem in children and adolescents worldwide [1,2]. It refers to a wide spectrum of liver diseases ranging from steatosis, when fat accumulates in the liver, nonalcoholic steatohepatitis (NASH), when fat in the liver causes liver inflammation, to cirrhosis, when chronic inflammation progresses to advanced scarring of the liver [3]. It is highly associated with obesity, which is becoming a serious public health problem globally, and in turn shifted the attention from steatosis in adults to children and adolescents in recent years [4]. It is also frequently associated with insulin resistance (IR), type 2 diabetes mellitus (DM), and dyslipidaemia, which are the main components of metabolic syndrome (MS) [5–7]. Most of the children diagnosed to have NAFLD (83.3%) presented with at least one feature of MS, whereas overt MS (i.e., more than three features) was present in 28.8% of them [8].

Reports of paediatric fatty liver disease have increased over the past decades. However, the actual prevalence of NAFLD in children remains unknown because of the lack of population-based studies and the lack of reliable concrete screening methods [2]. Fatty liver prevalence differs according to the country, the method of screening, the age range, and the clinical characteristics of the target population. Some of the available population-based studies of paediatric NAFLD suggest a prevalence of 7.1%, 4.4%, and 3.2% in Iran, Japan, and Korea, respectively [9–11].

The problem of fatty liver in Egyptian children has not been sufficiently studied in terms of prevalence and risk factors. Studying the risk factors behind the development of fatty liver in children is crucial for the development of a primary prevention programme

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aiming at modification of lifestyle in children at risk. Moreover, early detection of steatosis in children is mandatory for early intervention and prevention of further complications. The aim of the present study was to estimate the prevalence and determine the associated risk factors of fatty liver in the studied schoolchildren and to explore the ability of some obesity indices to predict fatty liver disease and consequently be used as a screening method for fatty liver disease at certain cutoff points in children.

Patients and methods

This study was a hospital-based cross-sectional, nested case–control study. The study participants were selected by simple random sampling from outpatient schoolchildren aged 6–18 years attending the radiology clinic for screening of fatty liver at the Sporting Health Insurance Paediatric Hospital in Alexandria. Children who were diabetics, had malignancies, on immunosuppressive therapy, and/or had a known liver disease or hepatitis C virus (HCV) infection by history were excluded from the study. The study comprised 800 students who were screened by ultrasonography (US) for the presence of NAFLD after getting their informed assent and their parents' written informed consent. Although liver biopsy is the gold standard for fatty liver diagnosis, its relatively high expense and invasiveness make it unsuitable for screening. Therefore, we used US for screening because of its low cost, noninvasiveness, safety, and absence of radiation exposure. We used a convex-type transducer of an ultrasound device with 3.5–5-MHz frequency. NAFLD was diagnosed according to the following features: [12,13] (a) the echo level of the liver in contrast to that of the kidney, (b) the clarity of the hepatic vessels, and (c) posterior attenuation and visibility of the diaphragm. Fatty liver was graded as follows. Grade 1 (mild): a slight diffuse increase in fine echoes in the hepatic parenchyma with normal visualisation of the diaphragm and intrahepatic vessel borders. Grade 2 (moderate): a moderate diffuse increase in fine echoes with slightly impaired visualisation of the intrahepatic vessels and diaphragm. Grade 3 (severe): a marked increase in fine echoes with poor or no visualisation of the intrahepatic vessel borders, diaphragm, and posterior portion of the right lobe of the liver. Age and sex were the only recorded data from the children during the initial screening. Among the US confirmed cases, only 75 children who agreed to continue in the study were further studied together with a similar number of age- and sex-matched controls who were free from fatty liver. Among the 75 fatty liver cases, 47 were mild and 28 were moderate but none were severe. A questionnaire was used to obtain information on sociodemographics, medical history, physical activities, and nutritional habits. Cases and controls were also subjected to complete anthropometric measurements and laboratory investigations.

Weight (kg) and height (cm) were measured and body mass index (BMI) and *Z*-score were calculated using the Child and Teen BMI Calculator [14]. BMI was calculated using the following formula (BMI = weight (kg)/(height (m))^2) [15]. The BMI-for-age percentile was used to interpret the BMI value which is age- and sex-specific for children and teens. The Centers for Disease Control and Prevention (CDC) BMI-for-age growth charts for girls and boys allow translation of a BMI number into a percentile for a child's or teen's sex and age [16]. The weight status category for the calculated BMI-for-age percentile was defined as follows: underweight (<5th percentile), normal weight (5th percentile to <85th percentile), overweight (85th to <95th percentile), and obese ($\geqslant$95th percentile). Waist circumference (WC; cm) was also measured at the umbilical level.

Blood samples were collected from the 150 children in the morning after 12 hours of fasting using the universal sterile precautions. Using the enzymatic colorimetric method, and measurement by spectrophotometry, plasma levels of fasting plasma glucose (FPG; Linear chemicals, Barcelona, Spain), alanine aminotransferase enzyme (ALT; Human, Wiesbaden, Germany), triglycerides (TG; Biosystems, Barcelona, Spain), high-density lipoprotein cholesterol (HDL; Biosystems, Barcelona, Spain), and cholesterol (Biosystems, Barcelona, Spain) were measured. Low-density lipoprotein cholesterol (LDL) level was calculated using the Friedewald (1972) formula [17]. Serum fasting insulin was measured using insulin ELISA Kit (LDN, Nordhorn, Germany). IR was calculated using the homeostasis model of insulin resistance (HOMA-IR) according to the following formula: [18] fasting Glucose (mg/dl) × fasting insulin (μU/ml)/405.

Children were diagnosed as having MS if they met at least three of the following criteria: (1) WC $\geqslant$90th percentile, (2) elevated blood pressures (BPs; systolic BP (SBP) and/or diastolic blood pressure (DBP) $\geqslant$90th percentile), (3) low HDL (<40 mg/dl) and/or high fasting serum TG ($\geqslant$120 mg/dl), and (4) high FPG ($\geqslant$100 mg/dl).

Ethical consideration

The study procedure strictly followed the international ethical consideration of the Helsinki Declaration. The study protocol was approved by the ethics committee of HIPH and students medical insurance sector in Alexandria.

Statistical analysis

Data entry and analyses were done using SPSS version 16. All statistical analyses were done using two-tailed tests and alpha error of 0.05 *p* value. Descriptive statistics were presented using frequencies as well as means and standard deviation to describe the categorical and numeric data, respectively. For comparing numeric parametric data, *t*-test was used. Mann–Whitney test was used to compare ranks (medians) for two independent groups of cases. Pearson's chi-square test was used to test for the association between the categories of two independent samples. Monte Carlo exact and Fisher's exact tests were used if there were many small expected values. Odds ratio (OR) and their confidence intervals (CIs) were used to assess the risk of NAFLD if a certain factor is present. Receiver Operating Characteristic (ROC) curve was used to test for the effect of some obesity indices (BMI, *Z*-score, and WC) on fatty liver and to have the optimal cutoff point (discriminating between groups) based on sensitivity and specificity for each selected point. This was created by plotting the fraction of true positives out of the positives (true positive rate, TPR) versus the fraction of false positives out of the negatives (FPR, false positive rate), at various threshold settings.

Results

Among the initially screened 800 students, 349 (43.6%) were boys and 451 (56.4%) were girls. NAFLD was diagnosed in 126 children giving a prevalence of 15.8%, 95% CI 13.2–18.3. Mild, moderate, and severe fatty liver represented 65.9%, 31.7%, and 2.4%, respectively of fatty liver cases. Prevalence of fatty liver increased significantly with age ($p = 0.004$) ranging from 8.7% for ages 6–10 years up to 20.4% for ages 15–18 years. Although there was no significant relation between gender and fatty liver ($p = 0.561$) in the overall population, a significant difference was noted in the oldest age group (15–18 years) where NAFLD was significantly associated with female gender (Fig. 1).

Table 1 shows the basic demographic characteristics, medical as well as family history of the 150 participants in the case–control study. It is well shown that both groups were matched with regard