Prevalence and risk factors for nonalcoholic fatty liver disease in obese children in rural Punjab, India

Nishu Gupta, Gunjan Jindal¹, Anuradha Nadda², Saloni Bansal³, Shailesh Gahukar⁴, Ashok Kumar⁵

Abstract:
BACKGROUND: Pediatric nonalcoholic fatty liver disease (NAFLD) is associated with insulin resistance, hypertension, metabolic syndrome, cardiovascular problems, and increased risk of chronic liver disease and Type II diabetes mellitus. The aim of the study was to assess the metabolic profiles and associated risk factors of NAFLD in obese children.

MATERIALS AND METHODS: Children with a body mass index (BMI) of >27 kg/m² an adult equivalent cutoff (Indian Academy of Paediatrics, 2015 guidelines) aged 5–18 years presenting to the pediatric outpatient unit of PGIMER Satellite Centre, Sangrur, India, were retrospectively recruited over a 1-year period. Anthropometry, lipid profile, thyroid levels, liver function test, fasting blood sugar, and blood pressure were measured. Ultrasonography was used to diagnose NAFLD. Logistic regression was used to assess the risk factors.

RESULTS: A total of 100 children participated in the study. The mean age was 10.6 ± 2.6 years and the mean BMI-Z score was 2.6 ± 0.5. The prevalence of NAFLD was 62%. Alanine transaminase (ALT) was significantly elevated in all the children with NAFLD. Lipid levels and BMI-Z-score were similar in both groups. Unadjusted odds ratio shows statistically significant association of ALT (2.058 [1.11–1.01]) and waist circumference (1.089 [1.19–0.99]) with NAFLD. With adjusted odds ratio only, ALT (1.12 [1.24–1.01]) was found to be significantly associated with NAFLD.

CONCLUSION: There is quite a high prevalence of nonalcoholic fatty liver in obese Indian children. All children with raised liver enzymes should undergo sonography to rule out NAFLD.

Keywords: Association, nonalcoholic fatty liver, obesity, risk factors

Introduction

Nonalcoholic fatty liver disease (NAFLD) is defined as hepatic fat infiltration of >5% by liver biopsy in the absence of any liver pathology and alcohol abuse. It can range from fatty infiltration alone to a triad of fatty infiltration, inflammation, and fibrosis known as nonalcoholic steatohepatitis. Pediatric NAFLD has a strong association with obesity, and children with NAFLD have a high prevalence of associated insulin resistance, Type II diabetes mellitus, hypertension, metabolic syndrome, and cardiovascular problems. These children are also at an increased risk of developing chronic liver disease and liver failure. The prevalence of pediatric NAFLD worldwide is in the range of 9%–37%. The increasing prevalence of fatty liver disease in children in developing countries has been noted as parallel to the increase in the prevalence of obesity in this part of the world. Potential interventions such as lifestyle and dietary modifications early in the course of disease can help in the prevention and/or reversal
Gupta, et al.: Prevalence and risk factors for pediatric NAFLD

In recent studies from India, a wide ranging prevalence of 26%-62.5% using ultrasonography (USG) as a diagnostic tool has been reported of pediatric NAFLD in obese children. A high proportion of overweight children with fatty liver on ultrasound indicates the increasing burden of this disease in the Indian pediatric population.

Although histopathology is the gold standard for detecting fatty liver changes, it is invasive with a high risk of associated complications. USG, a cheap and feasible in a low-resource setting, is a noninvasive method for the detection of the severity of steatosis and the grading of fatty infiltration in the outpatient department (OPD). The aims of the present study were to assess the metabolic profiles and associated risk factors of NAFLD in obese children using noninvasive screening methods.

Materials and Methods

A retrospective, observational assessment of a database of a pediatric outpatient unit of PGIMER Satellite Centre, Sangrur (Punjab), India, with a total of 100 children (aged between 5 and 18 years) was done over a 13-month period, between September 1, 2018, and October 31, 2019. Ethical approval was obtained from the Institutional Review Board/Ethics Committee (PGIMER, Chandigarh, functioning under the Ministry of Health and Family Welfare, Government of India) to conduct this retrospective study (record-based observational assessment), and written informed consent was taken from the parents of all participants in the study. Children aged between 5 and 18 years, resident in the Punjab for the last 5 years, with body mass index (BMI) of >27 kg/m² adult equivalent cutoff based on revised Indian Academy of Paediatrics (IAP) 2015 reference percentiles, and with all assessment details were included in the study.

Children with known liver pathology, history of familial hyperlipidaemia, storage disorder; children with obesity secondary to genetic, chromosomal, major endocrinal, metabolic syndrome; or children with psychological disorders, Children on medications that account for steatosis and those who were obviously short in stature were excluded from the study.

Sample size was calculated using the formula: $n = \frac{z^2 P (1 - P)}{d^2}$. The prevalence of pediatric NAFLD in overweight children had been estimated as about 45.6% as per an Indian study done in Haryana. Considering an absolute margin of error of 10% at 95% confidence interval with 90% power, the total sample size was 100. We enrolled consecutive 100 patients who fulfilled the inclusion criteria from the database for the study.

Baseline data on demographic and clinical characteristics were collected retrospectively throughout the study on a predesigned pro forma. Anthropometric assessments recorded were weight (kg), height (m), BMI (kg/m²), and waist circumference. BMI was measured as weight in kg divided by height in m². BMI Z-scores were calculated using revised IAP 2015 reference percentiles.

Obesity was defined as a BMI >27 kg/m² adult equivalent cutoff presented in the revised IAP 2015 BMI charts that had been proposed for Indian children, as Asian children are known to be prone to cardiovascular complications at lower BMI. BMI Z-scores were calculated. Waist circumference above 90th percentile for age and gender was considered as abdominal obesity.

Blood pressure (BP) readings were recorded from the data analyzed. Children with raised BP were labeled as hypertensive based on the BP reference given by Raj et al. Blood glucose, liver function tests, lipid profile, and thyroid profile readings were recorded from the data. ALT >26 U/l for boys and >23 U/l for girls were considered raised. Fasting and random sugar were considered elevated if they were ≥100 and 140 mg/dl, respectively. Triglycerides, total cholesterol, and low-density lipoprotein were considered high if ≥150 mg/dl, >200 mg/dl, and 130 mg/dl, respectively, and high-density lipoprotein (HDL) was considered low if <40 mg/dl in children of either gender. Normal values for thyroid hormones for the study were taken as per the pediatric reference intervals given by Kapelari et al. Abdominal ultrasound results were analyzed from the data retrospectively. Ultrasound Abdomen was done as a part of the routine workup for obese children presenting in the OPD. Ultrasound was done using Mindray DC 60 with 2–5 MHz convex probe on all obese children to determine the fatty changes in the liver, based on echogenicity of the liver in comparison to kidney, portal vein, and diaphragm. The size of the liver was also recorded from the data. Severity of fatty liver was routinely graded on USG reports in our institute as follows: Group A - normal liver, Group B - mild, Group C – moderate, and Group D - severe (as per the Needleman Criteria).

The data were entered in MS excel and analyzed using SPSS version 20 (IBM Corp., Armonk, NY, USA). Descriptive statistics (percentage, mean, median, and
mode) were calculated. Normality of data was calculated by Shapiro–Wilk test. Association of NAFLD with other risk factors was assessed by Chi-square test/McNemere’s test (categorical variable), Student’s t-test, and Mann–Whitney U-tests. Binary logistic regression was applied to calculate the odds ratio. Receiver operating characteristic (ROC) curve was constructed to discover the sensitivity and specificity of the screening tool. The level of significance was fixed at <0.05 at 95% confidence interval (CI).

Results

A total of 100 children were enrolled in the study. Of those, 62 (62%) were males and 38 (38%) were females. The mean age of males and females was 11.17 ± 2.8 and 9.93 ± 2.2 years, respectively, the mean BMI Z-score was 2.6 ± 0.5, and there was preexisting acanthosis nigricans in 78% of the patients. Twelve patients (12%) were found to have associated hyperglycemia while hypertension and subclinical hypothyroidism were found in 20% and 22% of the patients, respectively. Mean or median values of various biochemical and radiological parameters are presented in Table 1. The prevalence of NAFLD was 62% (presence of fatty infiltration on USG), of which 46% of patients had mild and 16% had moderate fatty infiltration. None of the patients was found to have severe fatty liver. A family history of obesity, diabetes, and hypertension was present in 42%, 34%, and 38% of the children, respectively [Table 1].

The risk factors found to have significance in relation to NAFLD were waist circumference and ALT level, whereas all other factors such as age, sex, and BMI were found to be statistically insignificant. Family history of obesity, diabetes, and hypertension was found not to be significant. Children with NAFLD had significantly raised levels of ALT and albumin as compared to children without NAFLD. But levels of total serum proteins, AST (Aspartate transaminase) and ALP (Alkaline phosphatase) were comparable in both the groups. Statistically no significant difference was found in the mean serum fasting sugars, thyroid hormones levels, and lipid levels between the two groups [Table 2]. Unadjusted odds ratio showed statistically significant association of ALT ≥28.5 U/l for boys and >23 U/l for girls (2.058 (1.11–1.01)) and waist circumference >90th percentile for age and gender (1.089 [1.19–0.99]) with NAFLD. With adjusted odds ratio only, ALT (1.12 [1.24–1.01]) was found to be significantly associated with NAFLD [Table 3].

To evaluate the potential of ALT (≥28.5 U/l) and waist circumference above 90th percentile for age and gender as a screening tool for NAFLD, an ROC curve was constructed. The area under the ROC curve for waist circumference ≥90th percentile for age and gender was 0.67 (95% CI 0.52–0.82, P = 0.05) and gave a sensitivity of 90% and a specificity of 84% for predicting NAFLD. The area under the ROC curve for ALT was 0.69 (95% CI 0.55–0.84, P = 0.02) and the cutoff of ALT ≥28.5 gave a sensitivity of 90% and a specificity of 90% for predicting NAFLD [Figures 1 and 2].

Discussion

The prevalence of NAFLD in obese pediatric patients in our study was 62% on ultrasound. Pawar et al. found the prevalence of NAFLD as 66.1% in overweight and obese children in a school-based cross-sectional study in Mumbai, which is consistent with our study. Irshad et al. and Das et al. documented NAFLD as 26% in obese

| Table 1: Characteristics of the study participants (n=100) |
|---------------------------------|------------------|
| **Characteristics**             | **N (%)**        |
| Age (years) Mean±SD             | 10.6±2.6         |
| Age- pubertal (9+ years)         | 69 (69.0)        |
| BMI Z score Mean±SD             | 2.6±0.5          |
| Comorbidities                   |                  |
| Hyperglycemia                   | 12 (12.0)        |
| Hypertension                    | 20 (20.0)        |
| Subclinical hypothyroidism      | 22 (22.0)        |
| Preexisting acanthosis nigricans| 78 (78.0)        |
| Biochemical parameters and liver size |
| Total serum cholesterol (mg/dl), Median (IQR) | 187.5 (155.7-206.2) |
| HDL (mg/dl) Median (IQR)        | 37.5 (34-43)     |
| LDL (mg/dl) Median (IQR)        | 143 (115.75-156) |
| VLDL (mg/dl) Median (IQR)       | 34 (30-39)       |
| Triglycerides (mg/dl) Median (IQR) | 184.5 (157.75-198) |
| AST (U/L) Median (IQR)          | 40.50 (32.75-54) |
| ALT (U/L) Median (IQR)          | 44 (37.75-54.25) |
| Fasting blood sugar (mg/dl) Mean±SD | 79.9±7.2        |
| ALP (U/L) Median (IQR)          | 217 (177.5-293.3) |
| Total protein (g/dl) Mean±SD    | 6.9±0.8          |
| Albumin (g/dl) Mean±SD          | 4.24±0.6         |
| TSH (μIU/mL) Mean±SD            | 4.13±1.6         |
| Total bilirubin (mg/dl) Mean±SD  | 0.45±0.2         |
| Liver size (cm) Mean±SD         | 14.06±2.2        |
| NAFLD grading by USG            |                  |
| Normal                          | 38 (38.0)        |
| Mild                            | 46 (46.0)        |
| Moderate                        | 16 (16.0)        |
| Severe                          | 0 (0)            |
| Family history                  |                  |
| Hypertension present            | 38 (38.0)        |
| Diabetes present                | 34 (34.0)        |
| Obesity present                 | 42 (42.0)        |
| Play hours/day                   |                  |
| 1                               | 46 (46.0)        |
| 2                               | 54 (56.0)        |

SD=Standard deviation, BMI=Body mass index, AST=Aspartate transaminase, ALT=Alanine aminotransferase, ALP=Alkaline phosphatase, HDL=High-density lipoprotein, LDL=Low density lipoprotein, NAFLD=Nonalcoholic fatty liver disease
The range of prevalence of NAFLD found in obese children in other developed countries varied widely from 26.0% to 85% in studies done by Yu et al. and Jimenez-Rivera et al. using USG and liver enzymes as screening tools. The wide ranging prevalence in these studies could be attributed to the different definitions of abnormal liver enzymes and different diagnostic criteria used in various studies. In our study, children with NAFLD were found to have significantly elevated ALT compared to children without NAFLD. The results of our studies also agreed with those of previous studies that evaluated the diagnostic accuracy of alanine aminotransferase (ALT) for NAFLD in children with obesity. Das et al. concluded that liver enzymes derangement was significantly higher in overweight children as compared to normal weight children in their study. Whereas ALT level was elevated in 35% of overweight children, only 1% of the normal-weight children had elevated ALT. Jimenez-Rivera et al. found that ALT was elevated in 61% of patients with NAFLD. Therefore, all children with raised liver enzymes should undergo sonography to rule out NAFLD. Similar to findings observed by Jain et al., in the present study, lipid levels were not statistically significantly different in the children with and without NAFLD though the Jain et al.’s study found lower levels of HDL.

### Table 2: Comparisons of clinical and biochemical parameters in children with and without nonalcoholic fatty liver disease

| Parameters                  | Children without NAFLD (n=38) | Children with NAFLD (n=62) | P-Value |
|-----------------------------|-------------------------------|----------------------------|---------|
| Age (years) Mean±SD         | 9.32±2.4                      | 10.52±2.2                  | 0.077   |
| <9                          | 18 (52.9)                     | 16 (47.1)                  | 0.105   |
| ≥9                          | 20 (30.3)                     | 46 (69.7)                  |         |
| Sex                         |                               |                            |         |
| Male                        | 22 (40.7)                     | 32 (59.3)                  | 0.445   |
| Female                      | 16 (34.8)                     | 30 (65.2)                  |         |
| Family H/O HTN              |                               |                            |         |
| Absent                      | 10 (32.3)                     | 21 (67.7)                  | 0.221   |
| Present                     | 9 (47.4)                      | 10 (52.6)                  |         |
| Family H/O DM               |                               |                            |         |
| Absent                      | 20 (30.3)                     | 46 (69.7)                  | 0.105   |
| Present                     | 18 (52.9)                     | 16 (47.1)                  |         |
| Weight (kg) Mean±SD         | 46.43±12.2                    | 54.2±14.4                  | 0.056   |
| Height (cm) Mean±SD         | 131.32±12.3                   | 137.63±13.1                | 0.096   |
| Waist circumference (cm) Mean±SD | 72.08±6.0              | 76.73±8.6                  | 0.045   |
| BMI Z-score Mean±SD         | 2.58±0.04                     | 2.54±0.4                   | 0.783   |
| BMI Mean±SD                 | 26.41±2.9                     | 28.10 (3.2)                | 0.065   |
| Liver size Mean±SD          | 13.89±1.4                     | 14.16±2.5                  | 0.679   |
| TP (g/dl) Mean±SD           | 6.83±0.6                      | 6.9±1.0                    | 0.764   |
| Albumin (g/dl) Median (IQR) | 4.1 (3.7-4.3)                 | 4.5 (3.9-4.7)              | 0.017   |
| AST/SGOT (IU/L) Median (IQR)| 36 (34-53)                    | 43 (32-56)                 | 0.337   |
| ALT/SGPT (IU/L) Median (IQR)| 39 (36-45)                    | 51 (38-67)                 | 0.024   |
| ALP (IU/L) Median (IQR)     | 209 (170-274)                 | 237 (187-308)              | 0.208   |
| T3 (ng/dl) Mean±SD          | 6.53±2.0                      | 1.44±0.25                  | 0.203   |
| T4 (ug/dl) Mean±SD          | 6.41±2.0                      | 6.47±3.2                   | 0.94    |
| TSH (uU/ml) Mean±SD         | 4.47±1.8                      | 3.93±1.4                   | 0.222   |
| Serum cholesterol (mg/dl) Median (IQR) | 200 (155-217)          | 172 (156-204)              | 0.384   |
| HDL (mg/dl) Median (IQR)    | 37 (34-43)                    | 38 (34-43)                 | 0.881   |
| LDL (mg/dl) Median (IQR)    | 145 (118-156)                 | 136 (109-156)              | 0.280   |
| TGs (mg/dl) Median (IQR)    | 187 (168-192)                 | 178 (156-199)              | 0.682   |
| FBS (mg/dl) Mean±SD         | 79.47±7.1                     | 80.16±7.4                  | 0.748   |

Statistical tests used: Independent t-test for comparison of means, Chi-square test/McNemer’s test for comparison of proportions, Mann-Whitney U-tests for median and IQR. IQR=Interquartile range, SD=Standard deviation, HTN=Hypertension, DM=Diabetes mellitus, BMI=Body mass index, TP=Total protein, AST=Aspartate transaminase, SGOT=Serum glutamic-oxaloacetic transaminase, ALT=Alanine aminotransferase, SGPT=Serum glutamic pyruvic transaminase, ALP=Alkaline phosphatase, TSH=Thyroid-stimulating hormone, HDL=High-density lipoprotein, LDL=Low-density lipoprotein, TGs=Triglycerides, FBS=Fasting blood sugar, NAFLD=Nonalcoholic fatty liver disease, H/O=History of
cholesterol in the adolescents with moderate or severe fatty liver. In the index study, 12% and 20% of the patients had associated hyperglycemia and hypertension. Findings are in agreement with the previous literature.\[16,19\] In addition, 22% of children had deranged thyroid profile in the form of subclinical hypothyroidism, a result which is in agreement with studies done by Stichel et al. and Reinehr et al., which also reported moderately increased peripheral thyroid hormones (T3 and T4) and TSH levels in obese children.\[20,21\]

However, as per a recent meta-analysis, TSH level could be an important risk factor for the development and progression of NAFLD, independent of thyroid hormones.\[22\] In view of the conflicting results of previous studies regarding thyroid dysfunction in NAFLD, further research is recommended to determine the relationship between thyroid dysfunction and NAFLD and the underlying mechanisms.\[23\]

Jain et al. found that the waist circumference standard deviation score SDS cutoff >1.4 had the highest discriminating ability, with the area under the ROC curve of 0.73 (95% CI 0.66–0.80), for predicting the risk of NAFLD similar to our study (area under the curve 0.67 [95% CI 0.52–0.82, P = 0.05]).\[6\] Although waist circumference was found not to be a significant predicting risk factor on adjusted odds ratio in our study [Table 3], this could be the result of the small sample size. This needs further evaluation as several earlier studies have also recognized waist circumference as a simple and effective screening tool for abdominal obesity and a means of identifying children at a higher risk of metabolic syndrome and cardiovascular diseases.\[24–27\]

The relatively small sample size and the nonavailability of the confirmatory tests such as liver biopsy and MRI are

### Table 3: Association of various factors with nonalcoholic fatty liver disease

| Factors                  | Unadjusted OR (95% CI) | P-value | Adjusted OR (95% CI) | P-value |
|--------------------------|------------------------|---------|----------------------|---------|
| ALT/SGPT (IU/L)          | 2.058 (1.11-1.01)      | 0.03    | 1.12 (1.24-1.01)     | 0.03    |
| Total cholesterol (mg/dl)| 0.996 (1.09-0.99)      | 0.50    | 0.989 (1.01-0.97)    | 0.37    |
| HDL (mg/dl)              | 1.019 (1.12-0.93)      | 0.68    | 0.918 (1.09-0.77)    | 0.33    |
| LDL (mg/dl)              | 0.988 (1.01-0.97)      | 0.21    | 0.975 (1.01-0.94)    | 0.17    |
| Triglycerides (mg/dl)    | 1 (1.02-0.98)          | 0.96    | 1.02 (1.06-0.98)     | 0.35    |
| Age <9 years             | 0.386 (1.29-0.12)      | 0.12    | 0.4 (1.94-0.03)      | 0.48    |
| Male sex                 | 0.776 (2.45-0.25)      | 0.67    | 0.646 (4.52-0.09)    | 0.66    |
| Waist circumference (cm) | 1.089 (1.19-0.99)      | 0.05    | 1.167 (1.42-0.96)    | 0.13    |
| BMI Z-score              | 0.836 (2.99-0.24)      | 0.77    | 0.785 (7.75-0.08)    | 0.84    |
| TSH (uIU/ml)             | 0.79 (1.15-0.54)       | 0.22    | 0.894 (1.56-0.51)    | 0.69    |

SD=Standard deviation, BMI=Body mass index, ALT=Alanine aminotransferase, SGPT=Serum glutamic pyruvic transaminase, TSH=Thyroid-stimulating hormone, HDL=High-density lipoprotein, LDL=Low-density lipoprotein, CI=Confidence interval, OR=Odds ratio
some of the limitations of present study. Although liver biopsy could have confirmed diagnosis of NAFLD, as the majority of the patients were asymptomatic and none was found with severe fatty infiltration on USG, liver biopsy was not indicated as per the treating physician.

**Conclusion**

The prevalence of nonalcoholic fatty liver in obese Indian children aged 5–18 years is rising, trend observed similar to the western countries. Early detection using various simple screening tools can go a long way in the prevention of chronic liver disease and associated comorbidities in the obese children. However, more population-based studies are recommended to find out the exact prevalence of the problem and definitive associations with various clinical and biochemical parameters.

**Financial support and sponsorship**

Nil.

**Conflicts of interest**

There are no conflict of interest.

**References**

1. Bellentani S, Marino M. Epidemiology and natural history of non-alcoholic fatty liver disease (NAFLD). Ann Hepatol 2009;8 Suppl 1:S4-8.
2. Parray AI, Zargar SA, Khan BA, Ahmad B, Saif RU, Kawoosa A, et al. Ultrasonographic prevalence of non-alcoholic fatty liver disease (NAFLD) in Kashmir valley school children. Int J Sci Res. 2015;2:299-33301.
3. Jou J, Choi SS, Diehl AM. Mechanisms of disease progression in nonalcoholic fatty liver disease. Semin Liver Dis 2010;30:283-91.
4. Hesham A-K 2008; 2:299-33301.
5. Schwimmer JB, Ugalde-Nicalo P, Welsh JA, Angeles JE, et al. Effect of a low free sugar diet vs. usual diet on nonalcoholic fatty liver disease in adolescent boys: A randomized controlled trial. JAMA 2019;321:256-65.
6. Jain V, Jana M, Upadhyay B, Ahmad N, Jain O, Upadhyay AD, et al. Prevalence, clinical and biochemical correlates of non-alcoholic fatty liver disease in overweight adolescents. Indian J Med Res 2018;148:291-301.
7. Das MK, Bhatia V, Sibal A, Gupta A, Gopalan S, Sardana R, et al. Prevalence of nonalcoholic fatty liver disease in normal-weight and overweight preadolescent children in Haryana, India. Indian Pediatr 2017;54:1012-6.
8. Indian Academy of Pediatrics Growth Charts Committee, Khadilkar V, Yadav S, Agrawal KK, Tamboli S, Banerjee M, et al. Revised IAP growth charts for height, weight and body mass index for 5- to 18-year-old Indian children. Indian Pediatr 2015;52:47-55.
9. McCarthy HD, Jarrett KV, Crawley HF. The development of waist circumference percentiles in British children aged 5.0-16.9 y. Eur J Clin Nutr 2001;55:902-7.
10. Raj M, Sundaram KR, Paul M, Deepa AS, Kumar RK. Obesity in Indian children: Time trends and relationship with hypertension. Natl Med J India 2007;20:288-93.
11. Schwimmer JB, Dunn W, Norman GJ, Pardee PE, Middleton MS, Kerkar N, et al. Safety study: Alanine aminotransferase cut-off values are set too high for reliable detection of pediatric chronic liver disease. Gastroenterology 2010;138:1357-64.
12. American Diabetes Association. Diagnosis and classification of diabetes mellitus. Diabetes Care 2014;37:S81-90.
13. American Academy of Pediatrics. National cholesterol education program report of the expert panel on blood cholesterol levels in children and adolescents. Pediatrics 1992;89:525-84.
14. Kapelari K, Kirchlechner C, Högl W, Schweitzer K, Virgolini I, Moncayo R. Pediatric reference intervals for thyroid hormone levels from birth to adulthood: A retrospective study. BMC Endocr Disord 2008;8:15.
15. Needleman L, Kurtz AB, Rilkin MD, Cooper HS, Pasto ME, Goldberg BB. Sonography of diffuse benign liver disease: Accuracy of pattern recognition and grading. AJR Am J Roentgenol 1986;146:1011-5.
16. Pawar SV, Zanwar VG, Choksey AS, Mohite AR, Jain SS, Surude KG, et al. Most overweight and obese Indian children have nonalcoholic fatty liver disease. Ann Hepatol 2016;15:853-61.
17. Yu EL, Golshan S, Harlow KE, Angeles JE, Durelle J, Goyal NP, et al. Prevalence of nonalcoholic fatty liver disease in children with obesity. J Pediatr 2019;207:64-70.
18. Jimenez-Rivera C, Hadijyanakkis S, Davila J, Hurteau J, Aglipay M, Barrowman N, et al. Prevalence and risk factors for non-alcoholic fatty liver disease in children and youth with obesity. BMC Pediatr 2017;17:113.
19. Kelishadi R, Cook SR, Adibi A, Faghihimaniz S, Ghatrehsmamani S, Beihaghi A, et al. Association of the components of the metabolic syndrome with non-alcoholic fatty liver disease among normal-weight, overweight and obese children and adolescents. Diabetol Metab Syndr 2009;1:29.
20. Stichel H, L’Allemand D, Gruters A. Thyroid function and obesity in children and adolescents. Horm Res 2000;54:14-9.
21. Reinehr T. Thyroid function in the nutritionally obese child and adolescent. Curr Opin Pediatr 2011;23:415-20.
22. Guo Z, Li M, Han B, Qi X. Association of non-alcoholic fatty liver disease with thyroid function: A systematic review and meta-analysis. Dig Liver Dis 2018;50:1153-62.
23. Ehsraghian A, Hamidian Jahromi A. Non-alcoholic fatty liver disease and thyroid dysfunction: A systematic review. World J Gastroenterol 2014;20:8102-9.
24. Taylor RW, Jones IE, Williams SM, Goulding A: Evaluation of waist circumference, waist-to-hip ratio, and the conicity index as screening tools for high trunk fat mass, as measured by dualenergy X-ray absorptiometry, in children aged 3-19 y. Am J Clin Nutr 2000;72:490-95.
25. Katzmarzyk PT, Srinivasan SR, Chen W, Malina RM, Bouchard C, Berenson GS. Body mass index, waist circumference, and clustering of cardiovascular disease risk factors in a biracial sample of children and adolescents. Pediatrics 2004;114:e198-205.
26. Moreno LA, Pineda J, Rodriguez G, Fleta J, Sarria A, Bueno M: Waist circumference for the screening of the metabolic syndrome in children. Acta Paediatr 2002;91:1307-12.
27. Morimoto A, Nishimura R, Kanda A, Sano H, Matsudaia T, Miyashita Y, et al. Waist circumference estimation from BMI in Japanese children. Diabetes Res Clin Pract 2007;75:96-8.