Table 1. Main clinical and biochemical characteristics of children/adolescents with biopsy-proven NAFLD, stratified by presence or absence of histologic NASH.

	Not NASH/borderline NASH (*n*=115)	With definite NASH (*n*=89)	*P* value
Age (years)	13.3 ± 2.6	12.8 ± 2.9	0.21
Male sex (%)	72.2	79.8	0.22
Weight (kg)	70.6 ± 18	70.5 ± 22	0.96
BMI (kg/m^2)	27.1 ± 4.5	27.5 ± 5.1	0.60
Waist circumference (cm)	93.8 ± 13	92.9 ± 16	0.67
Systolic blood pressure (mmHg)	116 ± 12	117 ± 14	0.36
Diastolic blood pressure (mmHg)	63 ± 11	73 ± 10	0.18
Fasting glucose (mg/dL)	86.1 ± 7	84.6 ± 6	0.12
Fasting insulin (mIU/L)	17 (13-21)	19 (13-28)	0.03
HOMA-IR score	3.6 (2.1-4.4)	4.1 (2.7-6.1)	0.03
Total cholesterol (mg/dL)	156 ± 32	156 ± 28	0.90
LDL cholesterol (mg/dL)	100 ± 30	98 ± 27	0.58
HDL cholesterol (mg/dL)	45 ± 9	46 ± 10	0.63
Triglycerides (mg/dL)	90 (69-128)	100 (70-123)	0.47
AST (IU/L)	26 (20-33)	28 (24-38)	0.01
ALT (IU/L)	28 (19-46)	33 (23-56)	0.04
GGT (IU/L)	15 (11-23)	17 (12-29)	0.05
Platelets (x 10^9/L)	334 ± 46	297 ± 64	<0.001
APRI score	0.20 (0.15-0.25)	0.25 (0.18-0.36)	<0.001
FIB-4 score	0.19 (0.15-0.23)	0.22 (0.17-0.27)	<0.001
PIIINP (ng/mL)	5.5 (2.6-6.8)	8.6 (4.7-11.4)	<0.0001
PNPLA3 variant, % (n)			
GG genotype	22.6 (26)	19.2 (17)	0.76
GC genotype	40.9 (47)	40.4 (36)	
CC genotype	36.5 (42)	40.4 (36)	

Simple size, n=204. Data are expressed as means±SD, medians (interquartile ranges, IQR) or percentages. Differences between the two groups were tested by chi-squared test for categorical variables, the unpaired *t*-test for normally distributed continuous variables, and the Mann-Whitney U test for non-normally distributed continuous variables (i.e., fasting insulin, HOMA-IR score, triglycerides, liver enzymes and PIIINP levels).

Abbreviations: ALT, alanine aminotransferase, APRI, AST to platelet ratio index; AST, aspartate aminotransferase; BMI, body mass index; FIB-4, fibrosis-4; GGT, gamma-glutamyltransferase; HOMA-IR, homeostasis model assessment-insulin resistance; PIIINP, N-terminal propeptide of type III collagen; PNPLA3, Patatin-like phospholipase domain-containing 3.

Table 2. Liver histology characteristics of children/adolescents with NAFLD, stratified by presence or absence of histologic NASH.

	Not NASH/borderline NASH (*n*=115)	With definite NASH (*n*=89)	*P* value
Steatosis grade, % (n)			<0.0001
<5%	5.2 (6)	0 (0)	
5% - 33%	40.9 (47)	23.6 (21)	
33% - 66%	53.9 (62)	56.2 (50)	
>66%	0 (0)	20.2 (18)	
Portal inflammation, % (n)			<0.0001
None	7.0 (8)	0 (0)	
Mild	72.2 (83)	35.9 (32)	
Moderate	20.8 (24)	64.1 (57)	
Lobular inflammation, % (n)			<0.0001
<2 foci per 200 x field	9.6 (11)	0 (0)	
2-4 foci per 200 x field	83.5 (96)	28.1 (25)	
>4 foci per 200 x field	6.9 (8)	71.9 (64)	
Ballooning, % (n)			<0.0001
None	13.0 (15)	0 (0)	
Few	79.1 (91)	29.2 (26)	
Many	7.9 (9)	70.8 (63)	
Fibrosis stage, % (n)			<0.0001
No fibrosis (stage 0)	7.0 (8)	0 (0)	
Perisinusoidal or periportal fibrosis (stage 1)			
1a mild, zone 3, perisinusoidal	55.7 (64)	37.1 (33)	
1b moderate, zone 3, perisinusoidal	6.1 (7)	1.1 (1)	
1c portal/periportal	24.4 (28)	20.2 (18)	
Perisinusoidal and periportal fibrosis (stage 2)	6.1 (7)	34.8 (31)	
Bridging fibrosis (stage 3)	0.8 (1)	6.8 (6)	
NAS score	3.4 ± 1.0	5.4 ± 0.6	<0.0001

Simple size, n=204. Data are expressed as either means±SD (for NAFLD Activity Score [NAS]) or percentages Differences between the two groups were tested by the Fisher exact' test for categorical variables and the unpaired *t*-test for continuous variables (i.e. NAS score).

Table 3. Association between plasma PIIINP levels and presence of histologic NASH in children/adolescents with biopsy-proven NAFLD.

	Odds Ratio	95% CI	*P* value
Unadjusted model			
PIIINP for 1-SD increment (i.e., 3.6 ng/mL)	2.75	1.92 – 3.94	<0.0001
Adjusted model			
PIIINP for 1-SD increment (i.e., 3.6 ng/mL)	2.72	1.87 – 3.98	<0.0001
Age (years)	1.00	0.88 – 1.14	0.94
Sex (male vs. female)	1.29	0.60 – 2.79	0.51
BMI (kg/m^2)	1.01	0.94 – 1.09	0.71
HOMA-IR score	1.23	1.03 – 1.47	0.02

Sample size, *n*=204. Data are expressed as odds ratios and 95% confidence intervals (CI) as tested by logistic regression analysis. The dependent variable for these logistic regression models was the presence of definite NASH on histology (n=89). Plasma PIIINP level was included for each SD increase.

Table 4. Association between plasma PIIINP levels and presence of fibrosis stage ≥2 in children/adolescents with biopsy-proven NAFLD.

	Odds Ratio	95% CI	*P* value
Unadjusted model			
PIIINP for 1-SD increment (i.e., 3.6 ng/mL)	11.8	5.75 – 24.1	<0.0001
Adjusted model 1			
PIIINP for 1-SD increment (i.e., 3.6 ng/mL)	14.5	6.24 – 33.8	<0.0001
Age (years)	1.06	0.88 – 1.30	0.52
Sex (male vs. female)	0.67	0.20 – 2.23	0.53
BMI (kg/m^2)	1.00	0.89 – 1.14	0.92
HOMA-IR score	0.84	0.63 – 1.11	0.22
Adjusted model 2			
PIIINP for 1-SD increment (i.e., 3.6 ng/mL)	14.1	5.50 – 35.8	<0.0001
Age (years)	1.07	0.88 – 1.31	0.48
Sex (male vs. female)	0.69	0.20 – 2.31	0.54
BMI (kg/m^2)	1.02	0.89 – 1.15	0.82
HOMA-IR score	0.86	0.64 – 1.14	0.29
NAS score	1.09	0.62 – 1.95	0.75
PNPLA3 variant			0.44
GC genotype	0.67	0.22 – 2.10	
GG genotype	1.65	0.45 – 6.02	

Sample size, *n*=204. Data are expressed as odds ratios and 95% confidence intervals (CI) as tested by logistic regression analysis. Two sequential multivariable logistic regression models are presented (*model 1*: adjusted for age, sex, BMI and HOMA-IR score; and *model 2*: adjusted for the same covariates of model 1 *plus* NAS score and *PNPLA3* rs738409 variant). The dependent variable for all these logistic regression models was the presence of mild/advanced liver fibrosis (F ≥2 fibrosis, n=45). Plasma PIIINP level was included for each SD increase.