Non-alcoholic fatty liver disease and eGFR levels could be linked by the PNPLA3 I148M polymorphism in obese children

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Background

The *patatin like phospholipase containing domain 3* (PNPLA3) I148M polymorphism has an effect on modulation of estimated glomerular filtration rate (eGFR) in non-obese non-diabetic adults and in children with histologically confirmed Non-Alcoholic Fatty Liver Disease (NAFLD).

Objective

To explored the impact of PNPLA3 I148M polymorphism on eGFR in obese children with and without NAFLD.

Methods

We genotyped 591 obese patients for PNPLA3 I148M polymorphism. Anthropometrical, biochemical and instrumental data were collected. NAFLD was defined by the presence of ultrasound detected liver steatosis and/or ALT levels >40IU/L.

Results

Patients with NAFLD showed significantly lower eGFR levels compared to subjects without NAFLD. Children with PNPLA3 MM genotype showed lower eGFR levels compared to those with either PNPLA3 IM or II genotypes both in presence and absence of NAFLD (Table1,2).
A general linear model for eGFR variance, including gender, duration of obesity, PNPLA3 genotypes, HOMA, BMI-SDS, LDL-C and triglycerides as covariates, was performed both in patients with (model r^2 0.29; model p=<0.0001) and without NAFLD (model r^2 0.14; model p=<0.0001). It confirmed an inverse association between eGFR and PNPLA3 genotype only in the NAFLD group (p-value of PNPLA3 genotypes=0.03 in patients with and 0.94 in patients without NAFLD) (Table 3).

	PNPLA3 II (n=152)	*PNPLA3* IM (n=123)	*PNPLA3* MM (n=52)	p-value
Age, yr	11.22±3.27	10.80±3.07	10.55±2.80	0.32
Duration of obesity	4.76±2.06	4.38±1.76	4.22±1.80	0.31
BMI -SDS	3.20±0.74	3.11±0.86	2.97±0.73	0.18
Sex (male), %	47.6	48.9	49.1	0.97
SBP-SDS	1.18±1.29	0.98±1.06	1.09±1.14	0.37
DBP-SDS	0.39±0.89	0.26±0.86	0.18±0.59	0.22
W/Hr	0.59±0.18	0.56±0.19	0.60±0.01	0.26
ALT, U/L	27.07±12.33	32.92±13.97	34.28±17.65	0.001
AST, U/L	25.21±10.52	27.90±11.12	29.10±9.38	0.01
GGT, U/L	20.21±9.20	21.10±10.31	19.98±10.71	0.41
Total-Cholesterol, mg/dL	156.53±29.60	161.61±30.50	153.13±24.36	0.16
LDL-C, mg/dL	92.23±22.86	87.55±21.73	97.70±24.32	0.04
HDL-C, mg/dL	44.66±11.22	45.78±11.62	45.09±10.15	0.73
Triglycerides, mg/dL	104.07±50.80	101.56±49.03	94.44±51.73	0.49
Glycaemia, mg/dL	79.62±9.20	82.67±8.55	79.84±6.97	0.11
HOMA-IR	6.95±6.57	6.08±4.10	5.95±4.82	0.37
eGFR, mL/min/1.73m²	185.64±47.49	167.27±20.92	161.93±22.35	0.0002

Table 1. Main features in patients with NAFLD according to *PNPLA3* genotypes

	PNPLA3 II (n=133)	*PNPLA3* IM (n=96)	*PNPLA3* MM (n=35)	p-value
Age, yr	10.62±3.11	10.79±3.11	9.82±3.24	0.30
Duration of obesity	4.92± 2.88	4.56± 1.50	4.38± 1.76	0.38
BMI -SDS	2.97±0.76	2.94±0.81	3.11±0.86	0.95
Sex (male), %	48.1	43.3	44.1	0.75
SBP-SDS	1.03±1.20	0.90±1.03	0.77±0.83	0.43
DBP-SDS	0.19±0.79	0.19±0.75	0.16±0.72	0.97
W/Hr	0.55±0.19	0.56±0.15	0.53±0.26	0.42
ALT, U/L	26.01±20.14	30.71±13.20	32.04±19.34	0.03
AST, U/L	20.72±5.04	21.57±4.68	22.14±6.38	0.29
GGT, U/L	17.49±5.66	17.13±4.78	17.11±3.75	0.87
Total-Cholesterol, mg/dL	163.07±28.25	162.48±28.80	158.21±21.99	0.67
LDL-C, mg/dL	92.26±21.53	97.67±27.52	91.27±21.87	0.31
HDL-C, mg/dL	49.03±14.77	48.26±14.59	50±17.32	0.86
Triglycerides, mg/dL	103.21±47.59	91.48±38.37	97.97±37.74	0.23
Glycaemia, mg/dL	79.58±7.49	79.99±8.11	78.40±8.84	0.62
HOMA-IR	5.29±4.27	4.82±3.39	3.54±1.81	0.08
eGFR, mL/min/1.73m²	183.30±48.08	169.31±22.46	162.02±27.95	0.01

Table 2. Main features in patients without NAFLD according to *PNPLA3* genotypes

NAFLD group			
Source	*Coefficient*	*F-ratio*	*p*
Model		5.51	<0.0001
Gender	-1.07	0.13	0.89
Duration of obesity	-6.7	3.2	0.002
PNPLA3 genotype	-12.3	2.12	0.03
HOMA	-1.65	1.5	0.14
BMI-SDS	13.1	2.87	0.005
LDL-C	0.36	1.87	0.06
Triglycerides	-0.01	0.07	0.94
Non-NAFLD group			
Source	*Coefficient*	*F-ratio*	*p*
Model		5.6	<0.0001
Gender	4.01	0.48	0.63
Duration of obesity	-1.15	0.71	0.48
PNPLA3 genotype	-0.37	0.07	0.94
HOMA	-1.6	1.53	0.13
BMI-SDS	12.07	2.35	0.02
LDL-C	0.03	0.19	0.85
Triglycerides	0.03	0.20	0.82

Table 3. GLM for analysis of variance for eGFR both in non-NAFLD and NAFLD group

Conclusions

Children with obesity and PNPLA3 MM genotype show lower eGFR levels compared to other genotypes, with a major effect of this polymorphism in the presence of NAFLD.

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