Mir-122 and non-alcoholic fatty liver disease in prepubertal obese children.

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Background

The incidence of non-alcoholic fatty liver disease (NAFLD) is dramatically increasing among children worldwide. The gold standard for diagnosis is the liver biopsy. Reliable serum markers are lacking. Recently, circulating miRNAs have been studied as biomarkers of disease progression. Specifically, miR-122 was proposed as predictive marker for liver disease in adults, while no data are available for children.

Objective: To investigate the relationship between circulating miR-122 levels and liver steatosis severity and metabolic parameters in obese children.

Methods

Antropometry, biochemical and metabolic assessment was performed in 50 prepubertal obese children (15 female, age 9.78 ± 2.17 yrs, BMI SDS 3.44 ± 1.39). Serum cytokeratin-18 (CK18) fragment, a novel biomarker of NAFLD, was determined by ELISA. In 44 subjects liver ultrasound was performed revealing no (n=19, group 0), mild (n=15, group 1), moderate (n=8, group 2), or severe steatosis (n=2, group 3). Serum levels of miR-122 were determined by qPCR.

	No steatosis	Mild steatosis	Moderate steatosis	Severe steatosis
Age (yrs)	9.9±2.2	9.8±2.2	10.2±2.1	9.8±2.5
F/M	6/13	4/11	1/7	0/2
BMI sds	3.4±1.4	3.4±1.4	3.3±1.2	3.6±1.8
Basal glucose (mg/dl)	78.8±8.5	78.5±8.2	77.1±7.9	82.3±8.9
Basal insulin (mcIU/ml)	17.3±11.5	16.9±11.1	15.7±7.4	24.5±19.8
Total cholesterol (mg/dl)	165.4±21.1	167.1±25.8	164.8±21.1	166.3±25.7
Triglycerides (mg/dl)	101.6±65.5	97.8±61.9	97.5±61.9	129±82.6
AST (UI/L)	31.7±10.2	31.2±9.7	32.1±9.5	31.9±14.6
ALT (UI/L)	33.3±18.7	32.5±17.7	35.8±19.3	32.5±19.4
CK18 (ng/ml)	110.7±30.9	120.6±66.9	154.8±64.4	227.7±99.7*
Mir-122	0.7±1.2	0.5±0.5	1.1±1.2	4.6±3.3*

Table 1. Clinical and biochemical parameters in patients according to the degree of steatosis.

Results

CK18 did not display a gender dimorphism, while miR-122 was higher in male subjects (1.06 ± 1.55 vs 0.28 ± 0.29, p 0.045). CK18 positively correlated with serum triglycerides (r=0.38, p=0.006), AST (r=0.54, p<0.0001), ALT (r=0.42, p=0.002), and GGT (r=0.26, p=0.07). miR-122 positively correlated with age (r=0.36, p=0.01), CK18 levels (r=0.40, p=0.006), AST (r=0.40, p=0.007), ALT (r=0.71, p<0.0001) and GTT (r=0.28, p=0.06) levels. After adjustment for age and sex correlations persisted. Serum miR-122 levels were higher in severe steatosis group when compared to the other groups (p<0.05). CK-18 levels were higher in severe steatosis group when compared to subjects without steatosis (p<0.05). There was a positive correlation between miR-122 levels and HOMA-IR, whereas no correlation was found for CK18.

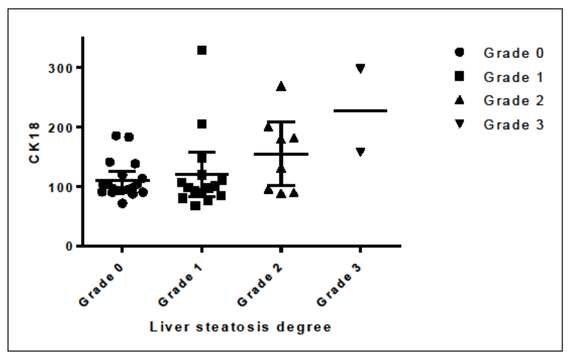

Figure 1. Comparation of CK-18 levels among patients with different degree of liver steatosis.

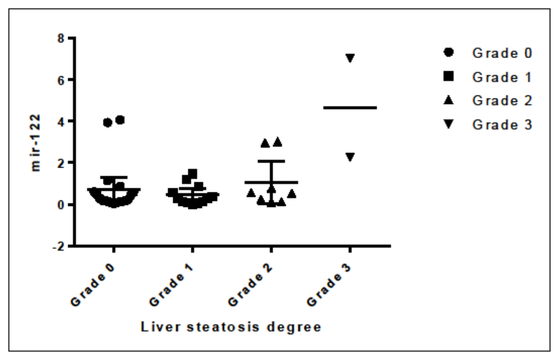

Figure 2. Comparation of mir-122 levels among patients with different degree of liver steatosis.

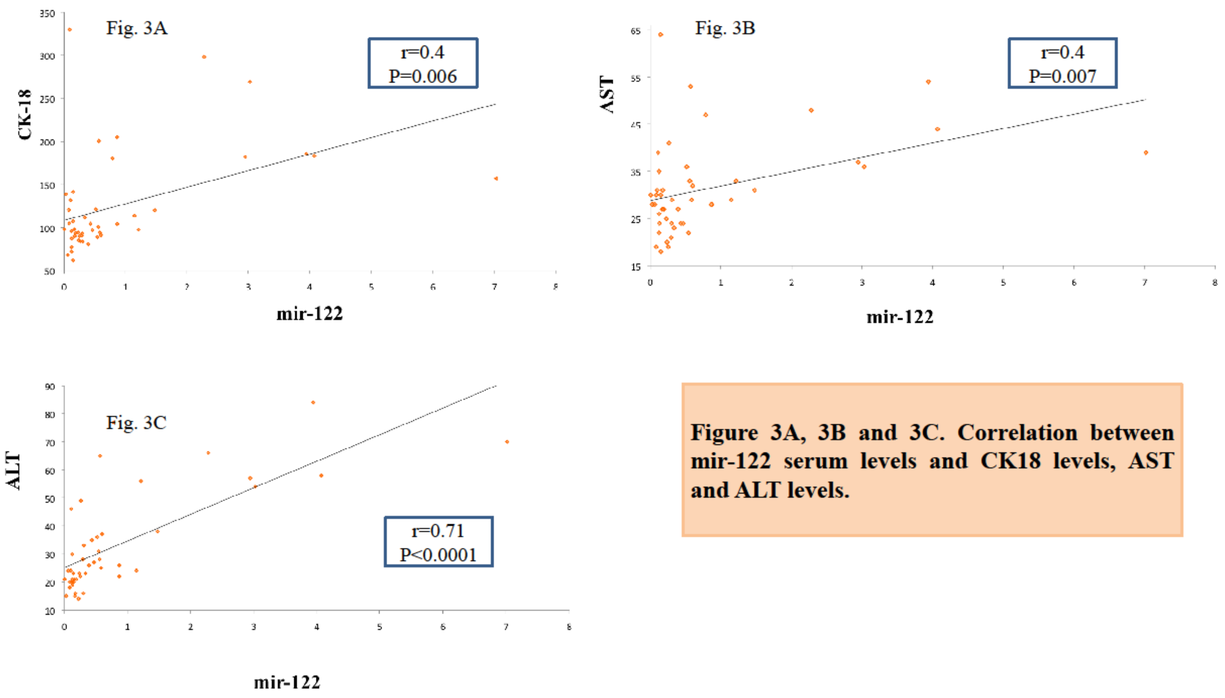

Figure 3A, 3B and 3C. Correlation between mir-122 serum levels and CK18 levels, AST and ALT levels.

Conclusions

In prepubertal children, miR-122 levels were associated with measures of liver disease. Further studies will elucidate if it provides a useful biomarker for liver disease progression in children.

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