Selenoprotein P levels discriminate the degree of hepatic steatosis and are related to the NAS score in patients with Non-Alcoholic Fatty Liver Disease

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1 INTRODUCTION

Alterations in glucose and lipid metabolism in the setting of insulin resistance (IR) play an important role in the progression from Non-Alcoholic Fatty Liver (NAFL) to Non-Alcoholic Steatohepatitis (NASH) via oxidative stress. Selenoprotein P (SeP) is a selenium carrier protein with antioxidant properties that is higher in obese and diabetic subjects but its potential role as biomarker of NASH is not fully elucidated yet [1-3].

2 AIM

The aim of this study was to assess the usefulness of SeP in discriminating NASH from simple steatosis in a well characterized cohort of biopsy proven NAFLD patients.

3 METHOD

- We studied 198 subjects with histological diagnosis of NAFLD.
- Plasma SeP levels were measured with a quantitative sandwich enzyme-linked immunosorbent assay (ELISA)
- Histology was scored according to Kleiner and NASH was defined by the joint presence of steatosis, ballooning and lobular inflammation

4 RESULTS

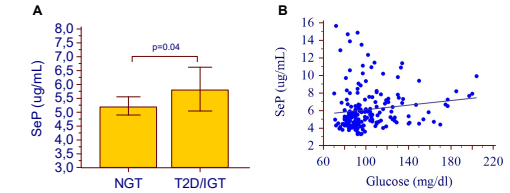
Clinical, biochemical and histological characteristics of the study cohort are reported in Table 1.

Table 1

Characteristics	N = 198
Age, y	47 ± 12
Gender, M/F	136/62
BMI, kg/m^2	28.6 ± 4.4
Waist, cm	99 ± 11
Type 2 Diabetes/IGT, n (%)	68 (34.3)
AST, UI/l	31 (30-34)
ALT, UI/l	53 (47-58)
Hb, g/dl	14.8 ± 1.4
PLT, x10^9/l	219 (213-226)
Albumin, g/dl	4.5 ± 0.4
Total Bilirubin, mg/dl	0.82 ± 0.87
c-peptide, ng/ml	2.84 ± 1.86
Fasting glucose, mg/dl	93 (92-97)
Fasting Insulin, uU/l	13.5 (11.8-16.6)
HOMA-IR	2.83 (2.36-3.48)
Total Cholesterol, mg/dl	189 (183-197)
HDL-Cholesterol, mg/dl	48 (46-49)
Selenoprotein P (ug/ml)	5.29 (5.0-5.63)
Histological features	
Fibrosis F0/F1/F2/F3/F4, n (%)	58/45/36/39/20 (29/23/18/20/10)
Steatosis, %	30 (25-35)
Steatosis grading S1/S2/S3, n (%)	106/65/27 (53/33/14)
Ballooning 0/1/2, n (%)	43/90/65 (22/45/33)
Lobular Inflammation 0/1/2, n (%)	34/145/19 (17/73/10)
NASH, n (%)	132 (66.7)

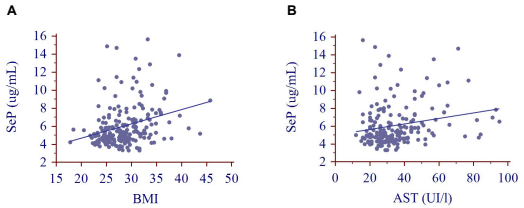
Overall, 68 (34.3%) subjects had type 2 diabetes and plasma SeP levels were significantly higher in diabetic/IGT patients compared to those without glucose abnormalities (**Figure 1A**). Accordingly, SeP levels significantly correlated with fasting glucose concentration (**Figure 1 B**).

Figure 1



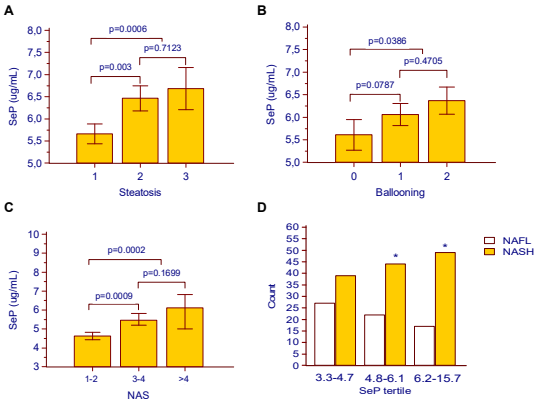
Circulating SeP mainly correlated with BMI (r=0.33, p<0.0001), AST (r=0.2, p=0.0022) and fasting plasma glucose (r=0.24, p=0.0009) **(Figure 2 A-B)**.

Figure 2



Among histological features, plasma SeP showed a stepwise increase according to hepatic steatosis grade and was able to discriminate mild (5-33%) from significant (≥33%) steatosis **(Figure 3A).** Furthermore, circulating SeP increased according to ballooning and NAS score (**Figure 3B-C**).

Figure 3



The prevalence of NASH was significantly higher in subjects who had SeP levels higher than 4.8 ug/ml **(Figure 3D)**.

4 RESULTS

At univariate regression analysis, BMI, AST, ALT, platelet count, iron, and hepatic steatosis were significantly associated with SeP levels but after multivariable regression analysis only BMI showed the best association (t = 3.56, p = 0.0005).
At univariate logistic regression analysis, SeP levels higher than 6,2 ug/ml were significantly associated with steatosis ≥ 33% (OR=2,9, 95% CI=1.5-5.3, p=0.0007) and NAS ≥ 5 (OR=2,5, 95% CI=1,3-4,8, p=0.0066).

5 CONCLUSIONS

Circulating SeP increased in NASH patients with diabetes and were associated to both hepatic steatosis and NAS score suggesting its potential role as biomarker in the setting of NAFLD.

6 ACKNOWLEDGEMENTS

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7 REFERENCES

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