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INTRODUCTION AND AIMS:

Nonalcoholic fatty liver disease (NAFLD) includes a wide spectrum of liver diseases ranging from steatosis to nonalcoholic steatohepatitis (NASH) and cirrhosis. On Hepatorenal Syndrome, portal hypertension triggers arterial vasodilatation in the splanchnic circulation and plays a central role in hemodynamic changes that lead to decline of renal function. The aim of this study is to investigate characteristics and evolution of kidney injury in NAFLD, correlation with biochemical markers, histological lesions, and probable risk factor on progression to Hepatorenal Syndrome.

METHODS:

126 NAFLD patients treated in a clinic for liver diseases were biopsied (108 NASH and 18 steatosis).

Severity of histological lesions (n)

| Histological lesions | Group I Ballooning | Group II Lobular inflammation | Group III Portal inflammation | Group IV Steatosis | Group V Fibrosis |
|----------------------|--------------------|-------------------------------|-------------------------------|--------------------|------------------|
| Grade zero | 4 | 22 | 14 | 5 | 6 |
| Grade 1 | 54 | 53 | 90 | 41 | 38 |
| Grade 2 | 68 | 37 | 22 | 35 | 53 |
| Grade 3 | 0 | 14 | 0 | 45 | 29 |

We analyzed the biochemical markers aspartate aminotransferase (AST), alanineaminotransferase (ALT) and Gamma-glutamyl transpeptidase (GGT). Creatinine clearance (Ccr) was calculated using the Cockcroft-Gault equation and patients were classified as presenting renal injury (< 90 mL/min) or hyperfiltration (> 130mL/min). Two tests were used to perform statistical analysis: the parametric unpaired t test and Fisher's Exact Test.

RESULTS:

We found no correlation with biochemical markers as well with NASH and Steatosis patients.

Patients - % and creatinine clearance

| Creatinine clearance | < 30ml/min | 60-89ml/min | 90- 130ml/min | >130ml/min |
|----------------------|------------|-------------|---------------|------------|
| % | 0.8 | 13.5 | 29.4 | 56.3 |

NASH and Steatosis patients - % and renal injury / hyperfiltration

| Creatinine clearance | < 30ml/min | 60-89ml/min | >130ml/min |
|----------------------|------------|-------------|------------|
| NASH (n=108) | 1 | 13.9 | 50.0 |
| Steatosis (n=18) | 0 | 16.7 | 57.4 |

CONCLUSIONS:

- 1- Ccr >130ml/min indicates precocious renal injury, since most NAFLD patients presented hyperfiltration and few patients presented low Ccr with no difference between steatosis and NASH.
- 2- Serial Ccr may be useful to predict evolution from inflammation to fibrosis.
- 3- Both portal and lobular inflammation may be considered as risk factors to renal injury.
- 4- Steatosis may be a risk factor for patients with severe histological grade.

Portal Inflammation grade vs Creatinine Clearance

| Portal Inflammation grade | Median Creatinine Clearance (minimum-maximum) | n |
|---------------------------|---|----|
| 0 | 97.4 (60.3-150.9) | 14 |
| 1 | 147.2 (61.6-338.4) | 90 |
| 2 | 122.0 (19.6-144.5) | 22 |

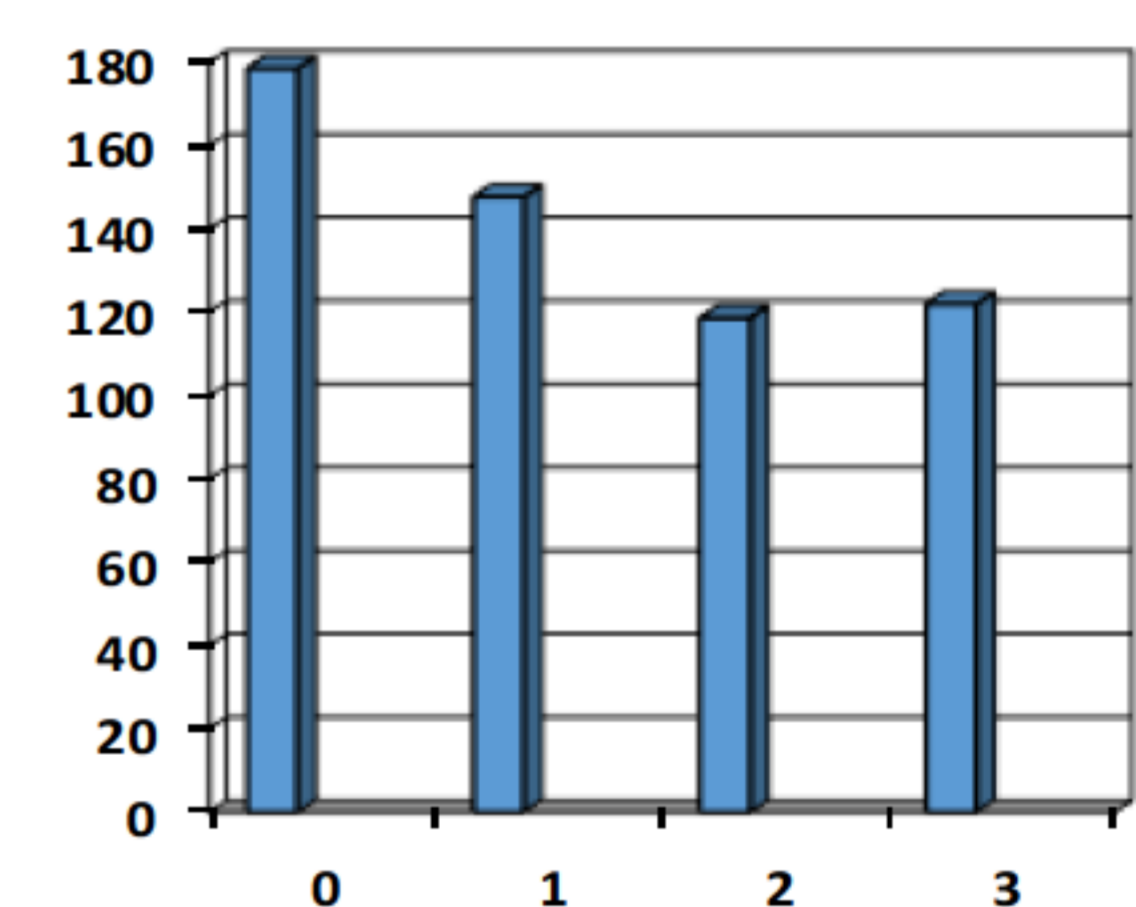
Portal Inflammation grade 0 X 1 p= 0.0027
 Portal Inflammation grade 1 X 2 p= 0.0016
 Unpaired t Test

Considering the histological grade, portal inflammation showed normal range of Ccr with evolution to hyperfiltration and, on lobular inflammation, hyperfiltration decreases to normal range.

Creatinine Clearance vs Lobular Inflammation grade

| Lobular Inflammation grade | Creatinine Clearance (minimum-maximum) | Patients |
|----------------------------|--|----------|
| 0 | 178.5 (60.3-296.3) | 22 |
| 1 | 147.7 (61.6-338.4) | 53 |
| 2 | 118.6 (19.6-237.0) | 37 |
| 3 | 122.0 (73.8-144.5) | 14 |

Lobular Inflammation 0 X 2 p < 0.0001
 Lobular Inflammation 0 X 3 p= 0.0006
 Lobular Inflammation 1 X 2 p= 0.0009
 Lobular Inflammation 1 X 3 p= 0.0231
 Unpaired t Test



Steatosis grade vs Creatinine Clearance

| Steatosis grade | Median Creatinine Clearance (minimum-maximum) | Total |
|-----------------|---|-------|
| 0 | 91.7 (72.5-124.9) | 5 |
| 1 | 136.9 (60.3-338.4) | 41 |
| 2 | 134.7 (19.6-271.1) | 35 |
| 3 | 140.5 (70.2-315.8) | 45 |

Steatosis grade 0 X 3 p= 0.0352
 Unpaired t Test