Table: summary of studies reporting association between non alcoholic fatty liver disease and thyroid dysfunction

Study Design Number Method for diagnosis Definition of thyroid Main Findings

of NAFLD/NASH dysfunction

Chung et al. (13) Cross-sectional 4648 (2324 Hypothyroidism Ultrasonography -Subclinical hypothyroidism: -Prevalence of NAFLD increased with severity of hypothyroidism (subclinical: 29.9 %, overt: 36.3%)

Versus 2324 euthyroidism) TSH>4.1mIU/L &normal fT4 -Prevalence of NAFLD plus elevated ALT was higher in patients with hypothyroidism (P<0.001)

-Overt hypothyroidism: -Hypothyroidism is an independent risk factor for increased prevalence of NAFLD

TSH>4.1mIU/L & fT4 <0.7ng/Dl (OR: 1.38, 95 % CI: 1.17-1.67)

Liangpunsakul et al. (14) Case-control 174 NASH patients compared Liver Biopsy Previous history of hypothyroidism - Prevalence of hypothyroidism was 15 % compared to 7.2 % in controls (P<0.001)

with 442 controls on T4 replacement therapy - In multivariate analysis, hypothyroidism was more prevalent than controls (OR: 2.3, 95 % CI:1.2-

4.2, P=0.008).

Silveira et al. (15) Cross-sectional 97 patients with NAFLD Liver Biopsy - TSH> 5 mIu/l or <0.3 miu/L - The prevalence of hypothyroidism in patients with NAFLD was 20 %.

Compared with 67 PBC - Total thyroxine>12.5µg/dL or <5 µg/dL - Five patients had hyperthyroidism in NAFLD group.

, & 79PSC - History of hyper/hypo thyroidism - The prevalence of thyroid dysfunction was not different in three group.

Pagadala et al. (16) Cross-sectional 233 patients with NAFLD Liver Biopsy - Clinical diagnosis of hypothyroidism - The prevalence of hypothyroidism was higher in NAFLD patients compared to controls (

Compared to 430 controls and on thyroid replacement therapy 21.1% vs.9.5%, P<0.001).

- Hypothyroidism was more common in NASH compared to patients without NASH. (P=0.03)

Xu et al. (17) Cross-sectional 227 patients with NAFLD Ultrasonography - TSH >4.5 mIU/L or <0.5 mIU/L - Patients with lower FT4 or higher TSH are more likely to develop NAFLD (P<0.001)

Compared with 651 controls - fT4 >14.4 pmol/l or <7.85 pmol/l - in logistic regression analysis Ft4 was a risk factor for NAFLD (OR: 0.847, 95 %CI: 0.743-0.966)

Mazo et al. (18) Retrospective 33 patients with steatosis Liver Biopsy - History of hypothyroidism on - Prevalence of hypothyroidism was 15.5 % in NAFLD (15.2 % in steatosis and 15.7 % in NASH)

Compared with 70 NASH patients thyroid replacement therapy - In multivariate analysis insulin, HOMA index and AST were correlated with hypothyroidism.

-No direct association between NASH and hypothyroidism

Moustafa et al. (19) Cross-sectional 90 patients with NASH, Chronic Ultrasonography -Only determined thyroid hormone - The serum TSH level in NASH patients was higher than healthy controls (2.1 ± 0.75 µIU/mL vs.

HCV, HCV cirrhosis compared to without normal range 1.75 ± 0.9 µIU/mL

20 healthy controls

Carulli et al. (20) Cross-sectional 69 NAFLD, 25 steatosis, 44 NASH Liver Biopsy - Normal range: TSH: 0.35-4.5µIU/mL - TSH level was significantly higher in NASH compared to steatosis group.

FT4: 6.1-16.6 pg/mL; - TSH level was an independent positive risk factor for NASH in logistic regression analysis (OR:

FT3: 1.7-4.2 pg/Ml 2.34, 95 % CI 1.15-4.776)

Zhang et al. (21) Cross-sectional 1322 participants including Ultrasonography - Normal TSH range: 0.71-6.25 mIU/ml - In female patient with NAFLD serum TSH level was significantly higher than controls (P<0.05).

266 patients with NAFLD - In logistic regression analysis TSH level was not an independent risk factor for NAFLD.

Ittermann et al. (22) Cross-sectional 3661 healthy appearing participants Ultrasonography - Thyroid hormone and TSH below or - Low FT4 concentrations are associated with hepatic steatosis

Above normal range - No consistent association between TSH and hepatic steatosis

- No association between hyper- or hypothyroidism and hepatic steatosis

Eshraghian et al. (23) Cross-sectional 832 healthy appearing participants Ultrasonography - Normal TSH range: 0.2- 5.2 mIU/ml - No association between hyper- or hypothyroidism and NAFLD

-FT4: 11.5-23 pmol/L - No association between thyroid autoimmunity and NAFLD

- The diagnosis of NAFDL was higher among low TSH group

- The thyroid hormone abnormalities may be due to sick euthyroid syndrome

TSH: Thyroid stimulating hormone, NAFLD: Non alcoholic fatty liver disease, NASH: Non alcoholic steatohepatitis, ALT: Alanine aminoteranspherase, PSC: Primary sclerosing cholangitis, PBC: Primary biliary cirrhosis