ANNALS of Hepatology

LETTER TO EDITOR

May-June, Vol. 12 No.3, 2013: 506-507

Decreased serum total T3 level in hepatitis B and C related cirrhosis by severity of liver damage

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Dear Editor:

I read with much interest paper by Mansour-Ghanaei, *et al.*,[1] about T3 level and cirrhosis severity. It provides useful information which consolidates previous evidence in this subject. However, there are some issues which may better clarify some details. I am thinking about why cases with previously known thyroid dysfunction or with clinical findings of thyroid disease have not been included in this study? Maybe they have had HBV or HCV at the time they were under treatment or when they were clinically symptomatic. We are not aware of the time of infection of HBV and HCV in most cases. By such criteria authors will lose some cases with more severe or more symptomatic thyroid disease that have HBV/HCV infection and may underestimate the strength of association between HBV/HCV and thyroid dysfunction.

Another issue is that how much has been the difference of T3 between cases with more severe disease (MELD > 20) and others? Only statistical significance is not important. Clinical significance should simultaneously be considered. Because of wider range of T3 in comparison with TSH and T4, the possibility of finding significance association/difference is higher for T3. This issue should be also considered for T3 in cases with and without bleeding varices.

Moreover, authors have five cases with hyperthyroidism as table 1 shows. What about these cases? Why they have only evaluated cases with hypothyroidism?

In addition, there are some statistical comments. Numbers are neither obvious nor exact index in statistics. It is preferred to use indices like odds ratio (OR) when we are comparing the severity of cirrhosis and number of cases with decreased T3 level. In such comparison, we can consider one group (for example cases with Child-Pugh score A) as reference group and compare other groups with this one. It is more informative.

Authors could consider MELD score as a quantitative index and do more advanced analysis like linear regression or ANCOVA. Considering quantitative variables as qualitative ones decrease the power and it can also be a cause for non-significancy between qualitative MELD (with a cutoff of 20) and T3 level.

It is advised to report power instead of P-value when the difference/association is not significant. So, we can have better idea that is the absence of difference/association due to lower sample size or it is more close to reality? In this study, comparison of thyroid indices other than T3 with severity of cirrhosis, and type of hepatitis (HBV or HCV) with serum levels of thyroid hormones, power (and not P-value) should be reported. Significancy says nothing in such cases.

Additionally, it is not obvious why authors have adjusted only for ascites when doing logistic regression? If they have considered P-value less than 0.05, as a criterion for including confounders in the model; here, P-value < 0.2 is preferred to 0.05.[2] Since, their logistic model has been adjusted for ascites, they should mention is OR of the association between ascites and low T3 a crude OR or adjusted for other variables in the model? Their logistic model needs more clarification.

Finally, I suppose P = 0.14 in abstract should be considered 0.014, as table 2 shows.

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Manuscript received: February 06, 2013.
Manuscript accepted: February 11, 2013.

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Author's replay:

Thanks for your interest in our report. We consent with the point that some matters should be clarified.

Thyroid diseases are manifested with changes in thyroid function tests and in our article the main aim was assessing the changes of thyroid function tests in patients with chronic liver disease and not in the patients with thyroid disease.

We assessed the patients in a period of time and in a cross sectional method and because cirrhosis of the liver due to HBV and HCV needs a long time, its onset was not the aim of our study.

In table 1 of our study[1] thyroid function tests were in three levels. The changes in thyroid hormones in this table don't illustrate thyroid diseases, but it is because of liver diseases and in fact these changes are measuring criteria for seriousness and progress of the illness. Non thyroidal illness syndrome, is also known as the low T3 syndrome or euthyroid sick syndrome, is not a true syndrome but it rather reflects alterations in thyroid function tests in a variety of clinical situations. Depending upon the etiology of the underlying nonthyroid illness, TSH levels may be low, but only on rare occasions are TSH levels undetectable due to just nonthyroidal illness alone. TSH may be transiently elevated even to > 20 mU/L during nonthyroidal illness recovery. Generally, decreases of serum T4 are seen in nonthyroidal illness and can be due to hypothalamic-pituitary suppression, disordered iodine uptake, abnormal peripheral metabolism, or decreased binding to carrier proteins such as thyroid hormone binding globulin (TBG). Measurements of free T4 are common within the normal reference range but may be low or slightly increased depending on the specific underlying disease process.[2]

After repeating analysis by logistic regression for comparing the severity of cirrhosis and T3 level, Child-Pugh score A (Score less than 7) were in one group and Child-Pugh score B and C (Score between7-10) were in other group. Variables under 0.2 were included in model. The results indicated that T3 level was significant ($P < 0.002$, OR = 17.8). Also by logistic regression for MELD score (with a cutoff of 20) and variables under 0.2 were included in model, T3 level was significant ($P < 0.05$, OR = 1.6).

We agree that after comparing the severity of hepatitis and thyroid function tests and type of hepatitis, power should be reported. We also agree that the relationship between MELD Score and T3 was significant ($P < 0.014$), it is a typographical mistake, and abstract should be corrected. We again thank you for your attention.

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