Original Research Article

A STUDY OF ALTERED THYROID HORMONES METABOLISM IN ALCOHOLIC LIVER DISEASES: AN ANALYTICAL STUDY

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ABSTRACT

Background
Alcoholic Liver Disease (ALD) is among one of the ten most common causes of deaths worldwide. Liver the largest gland in the body is a major site of thyroid hormones peripheral metabolism and is involved in its conjugation, biliary excretion, oxidative deamination and extrathyroidal deiodination of T_4 to T_3. In most chronic hepatic illnesses defects arise in thyroid hormone metabolism resulting in sick euthyroid syndrome. The above functions of liver are impaired in chronic liver diseases leading to decrease in T_3, T_4 and altered TSH levels. Some patients with chronic liver diseases may have thyroiditis, hyperthyroidism or hypothyroidism through autoimmune mechanisms. The exact mechanisms behind this is not well understood and hence the present study.

Methods
In the present study about 100 males subjects were selected randomly from Medicine OPD of GMCH, Nagpur in the age group of 40 – 60 years (50 normal healthy controls and 50 alcoholics) during May 2020 to May 2022. IEC approval was sought and informed consent was obtained from each subjects. Height, Weight of each subjects were measured by standing against a wall with a measuring scale on it and Body Mass Index (BMI) was calculated and recorded. After satisfying all inclusion and exclusion criterias about 5 ml of venous blood was withdrawn from each subjects ante-cubital vein using disposable sterile syringe and needle under strict aseptic precautions. The samples were immediately processed in ADVIA Centaur XP using chemiluminescence immunoassay technique for T_3, T_4 and TSH levels.

Using appropriate statistical methods (Student's paired-t-test, Pearson's correlation coefficient) data was analysed.

Results

It was observed that BMI in ALD (20.21 ± 2.2) was highly significantly decreased as compared to controls (23.06 ± 2.4) with p – value of < 0.005 [Chart 1.]. In ALD patients there was a highly significant decrease in T_3 (0.48 ± 0.08) and T_4 (6.4 ± 1.55) levels when compared to controls [T_3 (0.98 ± 0.33), T_4 (8.85 ± 1.79)] with p – value of < 0.005. While TSH levels (4.77 ± 0.7) in ALD was observed to be highly significantly raised when compared to controls (2.46 ± 0.8) with p – value of < 0.005 [Chart 2.].

Conclusions

In ALD patients a highly significant decrease in T_3 levels was seen due to decrease peripheral conversion of T_4 to T_3 may be due to decrease in activity of hepatic iodothyronine – 5'-deiodinase. Moreover, upon withdrawal of ethanol the already decreased TBG reverts back to normal. Acetaldehyde a thyrotoxic agent may cause a blunting TSH response to TRH resulting in altered thyroid hormone levels in ALD patients which may stress a need in better ALD patient management since patients are clinically euthyroid and Propylthiouracil remains the mainstay of treatment in hypothyroidism.

Keywords: ALD, BMI, ADVIA Centaur XP, T_3, T_4, TSH, TRH.

INTRODUCTION

Alcoholic Liver Disease (ALD) is among one of the ten most common causes of deaths worldwide, a major cause of mortality and morbidity in developing countries like India. Alcoholic liver disease has a wide spectrum, varying from asymptomatic liver enlargement to severe liver failure and or portal hypertension with high mortality rate. Quantity, frequency and duration of alcohol intake are the most important risk factor involved in the development of alcoholic liver diseases. Consumption of 160 g/d is associated with 25 fold increased risk of developing alcoholic cirrhosis. Chronic infection with hepatitis C is an important co-morbidity in the progression of alcoholic liver diseases to cirrhosis in chronic excessive drinkers.[1]

Thyroid gland is primarily involved in the synthesis of Thyroxine (T4) (normal: 110 nmol/day) which may be considered as a prohormone as about 80% of it gets converted to tri-iodothyronine (T3) (10 nmol/day) which is 4 -10 times more potent than T4 and has 10 times greater affinity than T4 to bind to nuclear receptors. Three groups of enzymes regulates thyroid metabolism forming part of iodothyronine-seleno-deiodinase enzyme system of which Type 1 is responsible for extrathyroidal monodeiodination of 30%– 40 % conversion of T4 to T3 in which there is sulfation of phenolic hydroxyl groups favouring inner ring deiodination instead of outer ring deiodination.[2]

Liver the largest gland in the body is a major site of thyroid hormones peripheral metabolism and is involved in its conjugation, biliary excretion, oxidative deamination and extrathyroidal deiodination of T4 to T3.[3] Liver is also involved in synthesis of Thyroxine binding Globulin (TBG), pre-albumin and albumin. In most chronic hepatic illnesses defects arise in thyroid hormone metabolism resulting in sick euthyroid syndrome.[2] Although almost all patients of liver diseases are clinically euthyroid. The above functions of liver are

impaired in chronic liver diseases leading to decrease in T3, T4 and altered TSH levels. Some patients with chronic liver diseases may have thyroiditis, hyperthyroidism or hypothyroidism through autoimmune mechanisms. The exact mechanisms behind this is not well understood and hence the present study.

AIMS AND OBJECTIVES

1. To estimate and compare T3, T4 and TSH levels in 50 ALD patients with that of 50 healthy controls.
2. To determine hypothetical mechanisms responsible for altered thyroid hormone levels in ALD patients.

MATERIALS AND METHODS

In the present study about 100 males subjects were selected randomly from Medicine OPD of GMCH, Nagpur in the age group of 40 – 60 years (50 normal healthy controls and 50 alcoholics).[4] during May 2019 to May 2022. IEC approval was sought and informed consent was obtained from each subjects. Height, Weight of each subjects were measured and BMI was calculated and recorded. After satisfying all inclusion and exclusion criterias (patients with clinical evidences of Diabetes Mellitus, renal diseases, hypertension, thyroid disorders, obesity and Non alcoholic staeto-hepatitis). About 5 ml of venous blood was withdrawn from each subjects using disposable sterile syringe and needle under strict aseptic precautions.[5] The samples were immediately processed in ADVIA Centaur XP using chemiluminescence immunoassay technique for T3, T4 and TSH levels.[6]

Principles of T3, T4 and TSH Estimations[6]

T3 essay: Competitive Immunoassay using Direct Chemiluminscent technology. T3 in the patients sample competes with a T3 analog, which is covalently coupled to paramagnetic particies in the Solid Phase for a limited amount of acridinium ester-labeled monoclonal mouse anti-T3 antibody in the Lite Reagent.

T4 assay: Competitive Immunoassay using Direct Chemiluminscent technology. T4 in the patients sample competes with a T4 analog, which is covalently coupled to paramagnetic particies in the Solid Phase for a limited amount of acridinium ester-labeled monoclonal mouse anti-T4 antibody in the Lite Reagent.

TSH assay: Two-site sandwich immunoassay using direct chemiluminometric technology, which uses constant amount of two antibodies. The first antibody, in the Lite Reagent, is a monoclonal mouse anti – TSH antibody labelled with acridinium ester. The second antibody, in the Solid Phase, is a polyclonal sheep anti – TSH antibody which is covalently coupled to paramagnetic particles.

Using appropriate statistical methods (paired-t-test, Pearson's correlation coefficient) data was analysed.[7]

OBSERVATIONS AND RESULTS

In Chart 1 it was observed that BMI in ALD (20.21 ± 2.2) was significantly decreased as compared to controls (23.06 ± 2.4) with p – value of < 0.004.

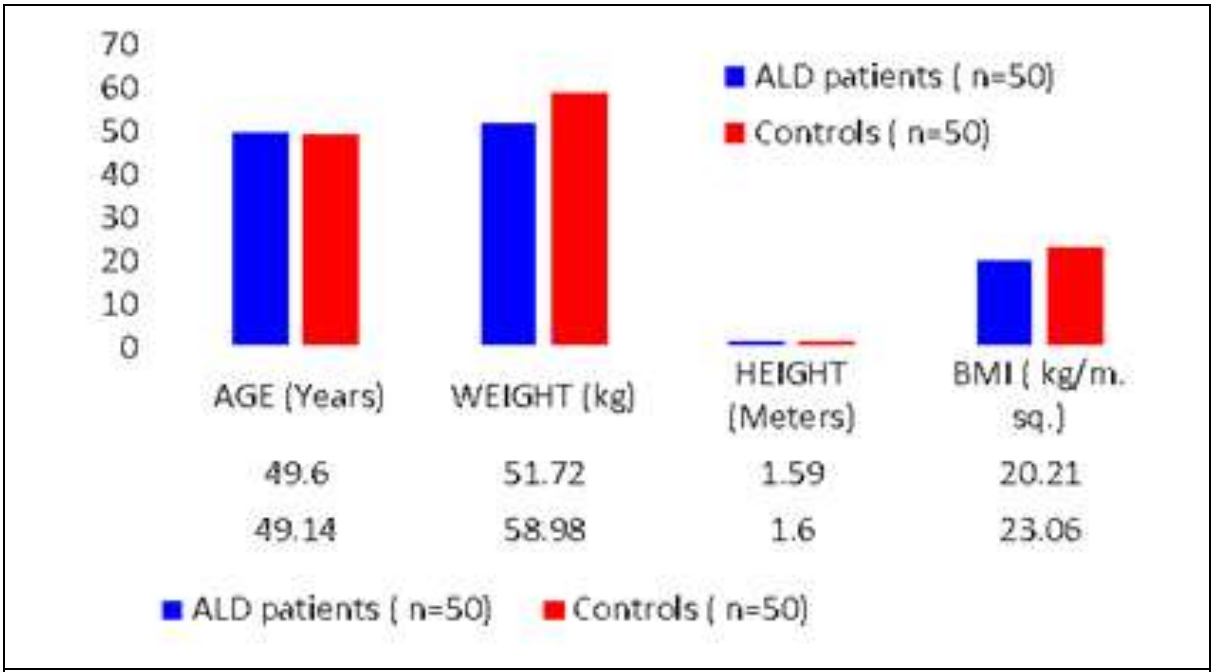

Chart 1: Distribution of age, weight, Height and BMI among ALD Patients and Controls

In ALD patients there was a highly significant decrease in T3 (0.48 ± 0.08) and T4 (6.4 ± 1.55) levels when compared to controls [T3 (0.98 ± 0.33), T4 (8.85 ± 1.79)] with p – value of < 0.005. While TSH levels (4.77 ± 0.7) in ALD was observed to be highly significantly raised when compared to controls (2.46 ± 0.8) with p – value of < 0.005 [Chart 2.].

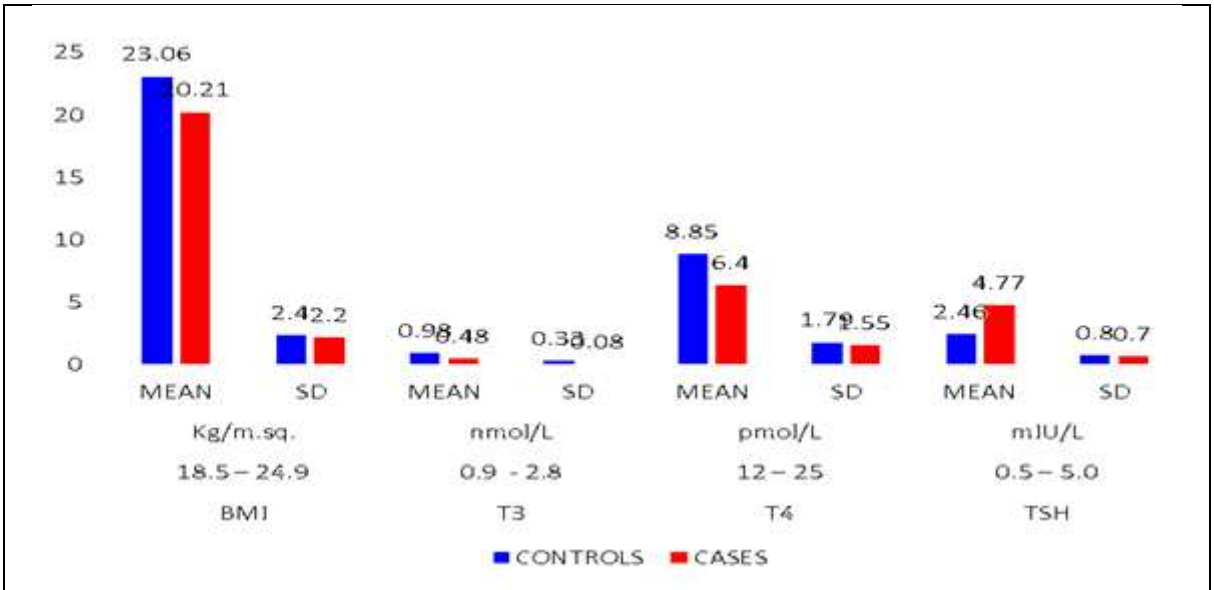

Chart 2: Mean ± SD of BMI, T3, T4, TSH among Controls and Cases

DISCUSSIONS

In the present study BMI in ALD patients (20.21) when compared to controls (23.06) was found to be significant with p-value of 0.004 (Chart 1). This findings was in accordance with the findings of Yi et al.[8]

In ALD patients there was a highly significant decrease in T3 (0.48 ± 0.08) and T4 (6.4 ± 1.55) levels when compared to controls [T3 (0.98 ± 0.33), T4 (8.85 ± 1.79)] with p – value of < 0.005. While TSH levels (4.77 ± 0.7) in ALD was observed to be highly significantly raised when compared to controls (2.46 ± 0.8) with p – value of < 0.005 [Chart 2.]. These fin dings are in accordance with findings of Hepner GW et al.[9]

In ALD patients a highly significant decrease in T3 levels was seen due to decrease peripheral conversion of T4 to T3 may be due to decrease in activity of hepatic iodothyronine – 5'- deiodinase. Moreover, upon withdrawal of ethanol the already decreased TBG reverts back to normal. The above findings are in accordance with Burra P et al, Chopra IJ et al, Geurts J, Demeester – Mirkine N et al.[10,11,12]

Dietary iodine in the form of iodide is completely absorbed from gastric and duodenal mucosa through sodium – iodide symporter (NIS) which gets damaged in patients of ALD leading to decrease iodine absorption resulting in its deficiency ultimately leading to decreased synthesis of thyroid hormones which may lands into hypothyroidism [13].

There is decresed synthesis of TBG due to impaired liver functions.[3]

Moreover acetaldehyde one of the intermediate metabolite of alcohol acts like a thyrotoxic agent which may cause a blunting TSH response to TRH resulting in altered thyroid hormone levels in ALD patients.[14] which may strass a need in better ALD patient management since patient's are clinically euthyroid and Propylthiouracil remains the mainstay of treatment in hypothyroidism.

CONCLUSIONS

In ALD patients a highly significant decrease in T3 levels was seen due to decrease peripheral conversion of T4 to T3 may be due to decrease in activity of hepatic iodothyronine – 5'-deiodinase. Moreover, upon withdrawal of ethanol the already decreased TBG reverts back to normal. Acetaldehyde a thyrotoxic agent may cause a blunting TSH response to TRH resulting in altered thyroid hormone levels in ALD patients which may stress a need in better ALD patient management since patients are clinically euthyroid and Propylthiouracil remains the mainstay of treatment in hypothyroidism.

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Conflict of Interest

None declared.

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