

EFFECT OF THYROIDECTOMY ON HEPATIC AND RENAL FUNCTION TESTS

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ABSTRACT

Background: The most common type of surgery associated with thyroid status is a thyroidectomy that generally is safe but it carries a risk of complications. **Aim:** This study estimates the direct effect of thyroidectomy on hepatic and renal biomarkers that measured quantitatively using the enzyme-linked immunosorbent assay (ELISA). **Materials and methods:** Totally, 90 individuals (45 thyroidectomy and 45 healthy) were selected from various hospitals in Nineveh, Baghdad and Wasit provinces (Iraq) during November (2022) to August (2023). Blood samples were collected, and the obtained sera were analyzed to measure the concentration of liver markers including the total protein, albumin, vitamin D, total bilirubin, ALP, ALT, AST and LDH as well as the renal markers including blood urea nitrogen and creatinine. **Results:** In comparison with the healthy, the findings of liver markers of thyroidectomy population were showed a significant elevation in values of albumin, A/G Ratio and ALT; while, significant reduction was seen in values of total protein and globulin. However, insignificant variation ($P>0.05$) was observed in values total bilirubin, globulin, vitamin D, ALP, AST and LDH. For kidney markers, although the values of BUN were increased significantly among the thyroidectomy individuals, no significant variation in creatinine values among the thyroidectomy and healthy individuals. **Conclusion:** The variable values of liver and kidney enzymes might indicate the alternative association of hyperthyroidism status prior to the surgery and / or the hypothyroidism effect after it. Thus, this study recommends that liver and kidney tests must be evaluated in individuals of thyroid dysfunction. Also, we suggested that various endogenous proteolysis might be related with thyroidectomy due to changes in levels of thyroid hormones (hypothyroidism or hyperthyroidism).

INTRODUCTION

Thyroid is a small, butterfly-shaped gland located at the anterior part of the neck under the skin (Mokle & Sanap, 2023). This gland is a part of endocrine system which plays a role in controlling many different important functions through producing and releasing certain hormones including triiodothyronine (T3), thyroxine (T4), reverse-triiodothyronine (rT3) and calcitonin. The main roles of these hormones are affecting on metabolism, digestion, body temperature, brain development, skin and bone maintenance and fertility (Alenezi & Elgazzar, 2022; Grebe, 2019). However, concentration of thyroid hormone is controlled mainly by the hypothalamus secretion; thyroid releasing hormone (TRH) activates thyroid follicular tissue to releasing T3 and T4 in presence adequate amount of iodine (Feldt-Rasmussen, Effraimidis, & Klose, 2021). Nonetheless, a variety of disorders could occur in thyroid gland to produce very low (hypothyroidism) or greater than normal (hyperthyroidism) amounts of thyroid hormone in addition to other disorders such as Hashimoto's thyroiditis, thyroid tumors and cancers

(Pirahanchi, Toro, & Jialal, 2018; Vanderpump, 2019). The most common type of surgery associated with thyroid disorders is a thyroidectomy that known as surgical removal of all or a part of thyroid gland. In general, thyroidectomy is a safe action; however, risk of complications like permanent hoarses, low concentration of parathyroid hormone, secondary infections and bleeding might be seen as with any surgery (Sakr & Sakr, 2020; Sawant et al., 2019).

Liver is the largest solid organ in the body, which is a part of accessory gland of digestive system and play a remarkable role in removing of toxic materials from blood, regulation of clotting factors, maintaining glucose level in blood, and performing many of other vital functions (Black, Termanini, Aguirre, Hawksworth, & Sosin, 2018; Thangam & Thirumurugan, 2022). Usually, liver considers a hormone-independent organ having a complicated association with thyroid gland in both healthy and diseased individuals (Bano et al., 2020; Piantanida et al., 2020). Kidney is a bean-shaped organ which considers as a part of urinary system and plays a role in filtration of blood, acid-base balance, and production of proteins such as renin, and hormones like calcitriol and erythropoietin (Reddi, 2020; Sobirjonova, Mahammadazimova, & Djuraeva, 2024). For many years, interaction between kidney and thyroid is known as the thyroid dysfunctions affecting the physiology and development of kidney, while renal disorders might be resulted in thyroid dysfunctions (Rezaei et al., 2019; Zhang et al., 2018). Disorders of the thyroid and kidney may co-exist with common in etiological factors, and treatment strategies (Al-majedy, 2021).

In Iraq, various studies have been conducted to detect the impact of thyroidectomy on liver function (Al-Janabi, Hassan, & Al-Fahham, 2022; Al-Khayyat, 2021; Jouda, Maghtoof, Alubadi, Kamil, & Qasim, 2019) and association with kidney diseases (Al Fahdi, Al Salmi, Al Rahbi, Shaheen, & Hannawi, 2022; Luaibi, Falhi, & Alsaedi, 2021; Sama, Jabbar, & Ali, 2020). However, no available online studies investigate association between thyroidectomy and liver / kidney functions. Therefore, this study aims to detect partially the direct effect of thyroidectomy on hepatic and renal biomarkers that measured quantitatively using the quantitative ELISA.

METHODOLOGY

Ethical approval

The current study licensed by the Scientific Committee of the Department of Biology, College of Education for Girls, University of Mosul (Nineveh, Iraq). All study individuals were agreed orally for obtaining the blood samples to performing this study.

Samples

Totally, 90 individuals (45 thyroidectomy and 45 healthy) were selected randomly to the current study from various official and private hospitals in Nineveh, Baghdad and Wasit provinces (Iraq) during November (2022) to August (2023). Each individual was subjected to draining 5 ml of venous blood into free-anticoagulant glass gel tube (AFCO, Jordan) throughout 7 days of surgery. After centrifugation (5000 rpm, 5 minutes) of blood samples, the obtained sera were kept into labeled Eppendor tubes that saved at -20°C into dark plastic container until their analysis, serologically.

Biochemical analysis

Following the manufacturer instructions of quantitative ELISAs kits (SunLong Biotech, China), the hepatic [total protein, albumin (A), vitamin D, total bilirubin, ALP (alkaline phosphatase), ALT (alanine transaminase), AST ([aspartate aminotransferase](#)) and LDH (lactate dehydrogenase)] and renal [BUN (blood urea nitrogen) and creatinine] markers were measured at 450 nm using the Automated Microplate Photometer (BioTek, USA). The concentration of

each marker was calculated by plotting the ODs of standards and sera with the concentrations of standard in the standard curve. Globulin (G) and A/G ratio were calculated based on the results of total protein and albumin.

Statistical analysis

The *t*-test in the GraphPad Prism Software (*version* 6.0.1) was applied to detect significant differences between the values [Mean \pm Standard Deviation (M \pm SD)] of thyroidectomy and healthy individuals at a level of significance equal to $P < 0.05$ (AL-Shaeli et al., 2022).

RESULTS AND DISCUSSION

Hepatic markers

In comparison with the values of healthy individuals, the findings of thyroidectomy group were showed a significant elevation ($P < 0.05$) in values of albumin (Figure 1), A/G Ratio (Figure 2) and ALT (Figure 3); while, significant reduction ($P < 0.05$) was seen in values of total protein (Figure 4) and globulin (Figure 5). However, insignificant variation ($P > 0.05$) was observed in values total bilirubin (Figure 6), vitamin D (Figure 7), ALP (Figure 8), AST (Figure 9) and LDH (Figure 10).

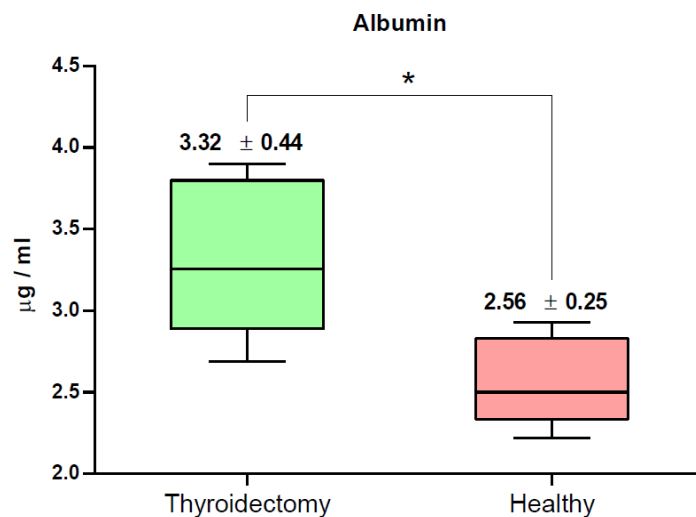


Figure (1): Albumin concentration in study population

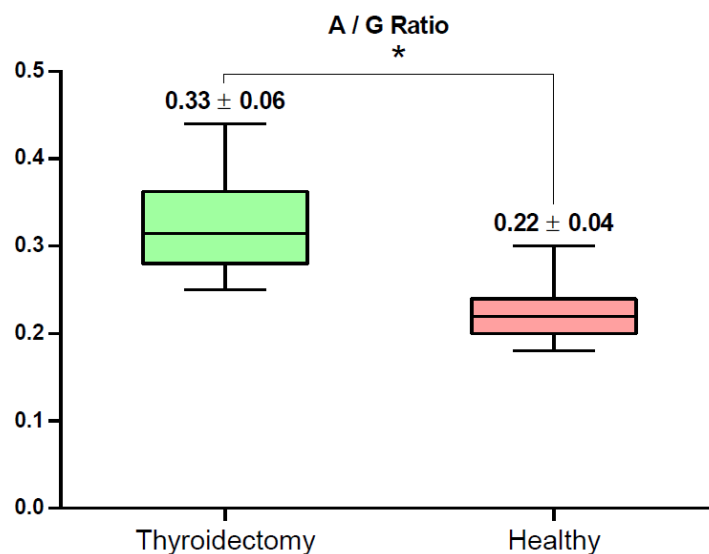


Figure (2): Levels of A/G Ratio in study population

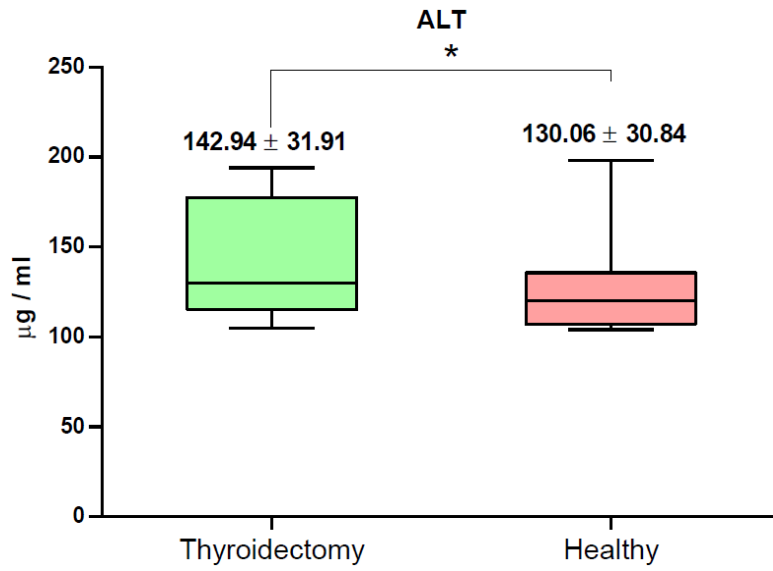


Figure (3): ALT concentration in study population

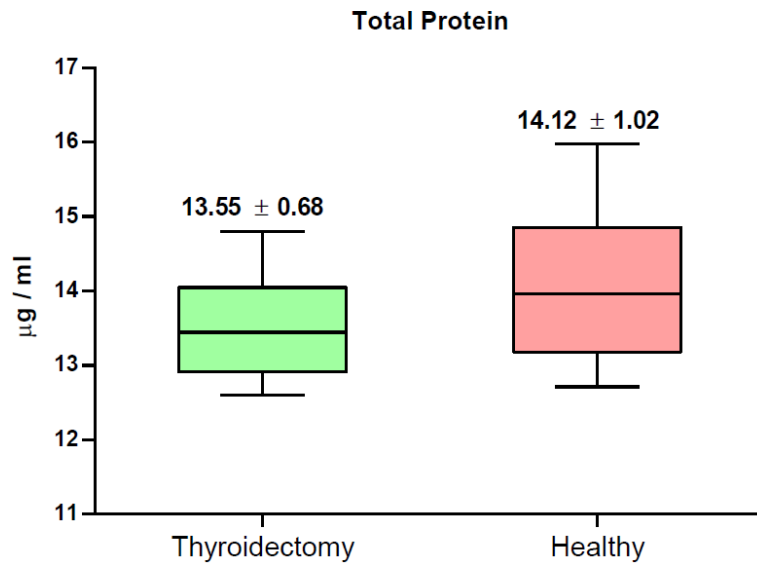


Figure (4): Total protein concentration in study population

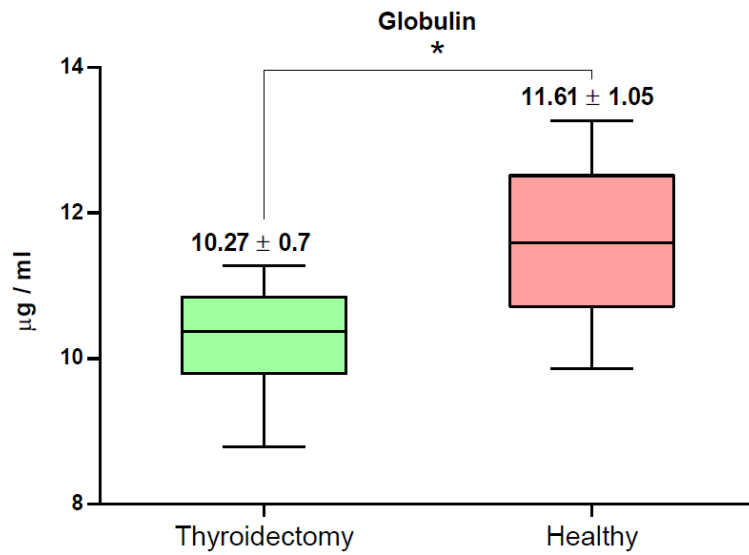


Figure (5): Globulin concentration in study population

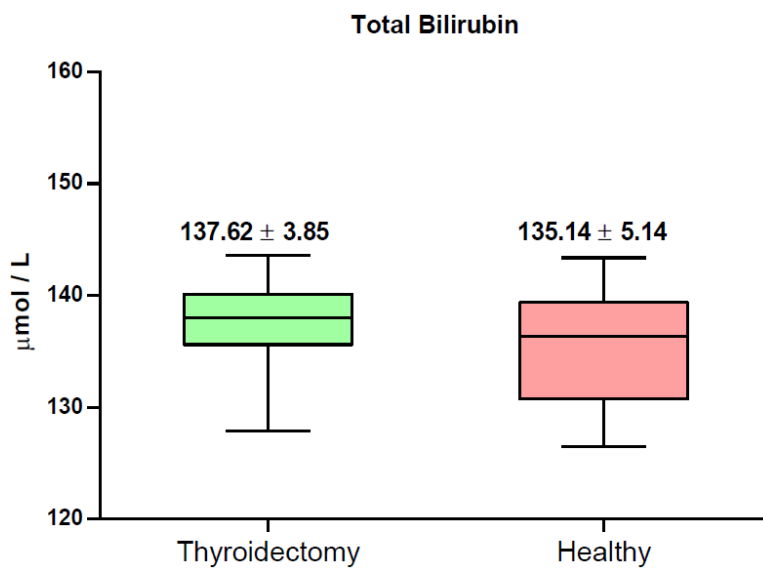


Figure (6): Total bilirubin concentration in study population

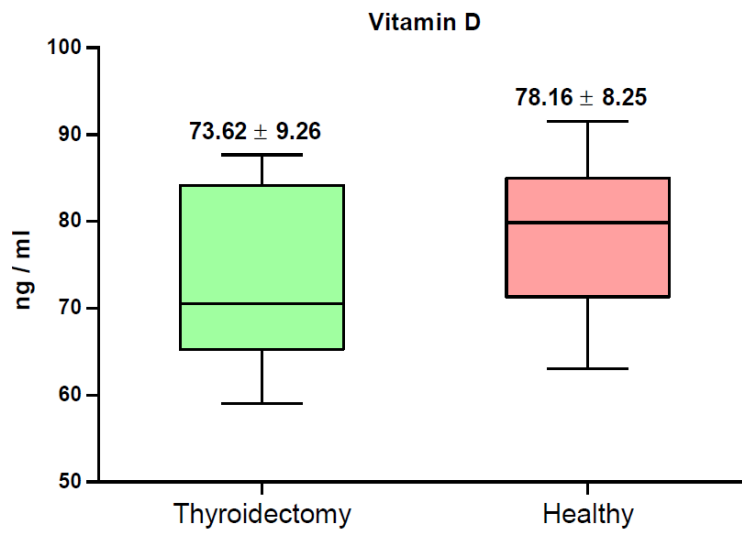


Figure (7): Vitamin D concentration in study population

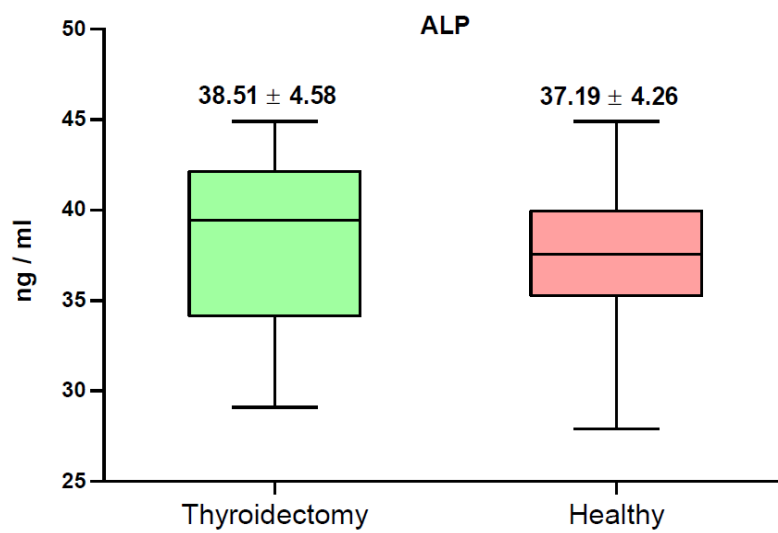


Figure (8): ALP concentration in study population

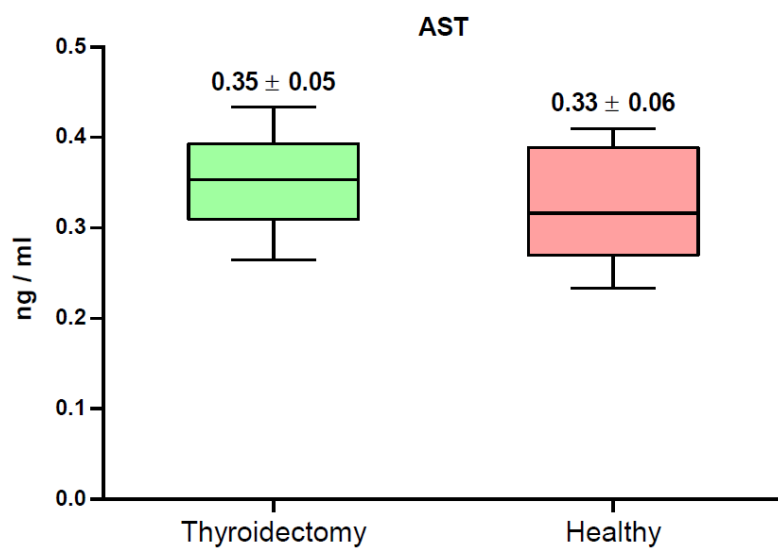


Figure (9): AST concentration in study population

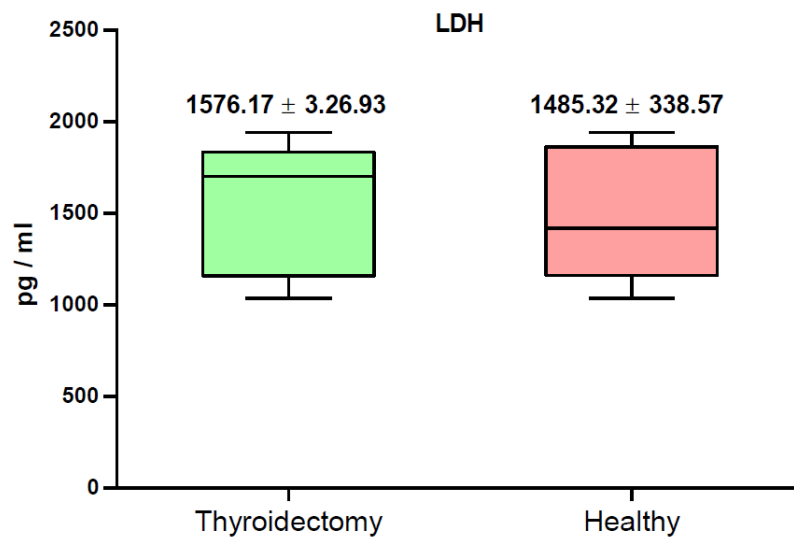


Figure (10): LDH concentration in study population

Renal markers

Although the values of BUN were increased significantly ($P < 0.05$) in thyroidectomy individuals (Figure 11), insignificant variation ($P > 0.05$) in values of creatinine was seen in comparison between the thyroidectomy and healthy individuals (Figure 12).

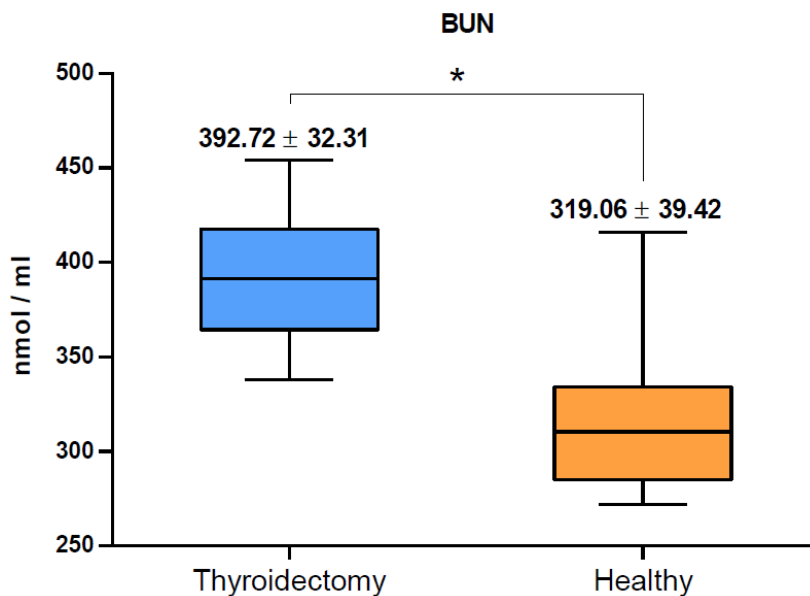


Figure (11): BUN concentration in study population

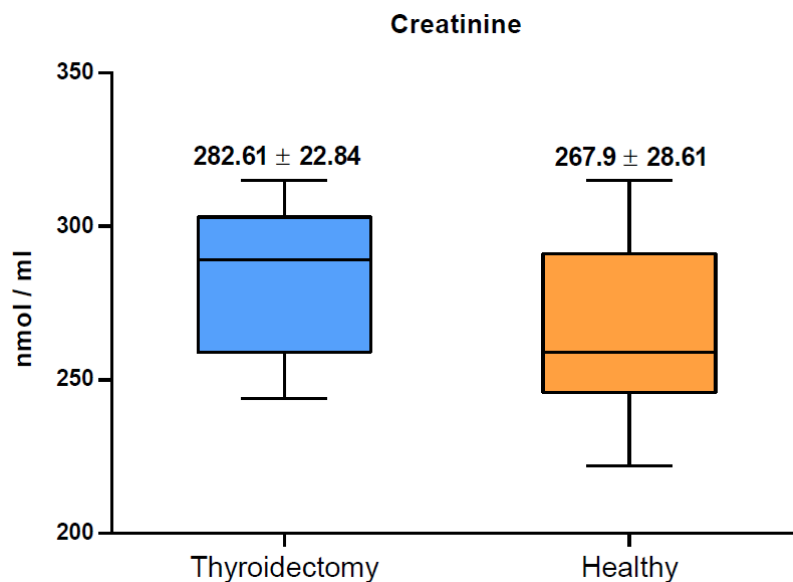


Figure (12): Creatinine concentration in study population

Discussion

Hepatic markers

The effect of hypothyroidism and hyperthyroidism on liver markers was varied significantly between the conducted worldwide studies. (Piantanida et al., 2020) reported the presence of complicated association for liver and thyroid in healthy and diseased individuals as liver acting many necessary physiological roles during activation of thyroid hormone, transporting and metabolism; *vice versa*, thyroid hormones affecting activity of hepatic metabolism and hepatocytes. In a previous report, researchers have been demonstrated the association of thyroid dysfunctions to frequent hepatic disorders as a result of excessively overloading of iron storage within the hepatic tissues (Oren, Brill, Dotan, & Halpern, 1998). In the different types liver disease, similar processes may occur to those seen in the sick euthyroid syndrome, but in addition a number of changes, specific to the type or stage of liver disease, are also found (Aatif, Qamar, Ahmed, & Imran, 2008). In a cross-sectional study, the findings showed that subclinical hypothyroidism is closely associated with non-alcoholic fatty liver disease (NAFLD) and cases confirming association of these two studies (Chung et al., 2012). (Ajala, Ogunro, & Fasanmade, 2013) observed that the positively correlation for hepatic markers to thyroid hormones and *vice versa*, with marked increasing the concentrations and activity of liver enzymes and total bilirubin in hypothyroid and hyperthyroid subjects. Other study showed an association of overt hypothyroid with significant derangement in biochemical parameters of liver function including raised serum total protein, ALT, AST and ALP (Yadav et al., 2013). (Deepika, Veeraiyah, Rao, & Reddy, 2015) demonstrated the marked elevation of total bilirubin, involving the direct and indirect, with increasing the concentrations of ALT, AST, ALP and globulin; however, the levels of total protein and albumin were reduced insignificantly.

(Ritter, Amano, & Hollenberg, 2020) concluded that thyroid hormone plays a marked effect in maintaining of liver homeostasis and insulin sensitivity. In hyperthyroidism, significant elevation in basal hepatic glucose production, gluconeogenesis and glucose utilization was seen (Al-bayati & Al-Khateeb, 2021; Mitrou, Raptis, & Dimitriadis, 2010). (Scappaticcio et al., 2021) detected the common prevalence of abnormal liver tests in untreated newly diagnosed hyperthyroid patients in particular ALT, AST, ALP, total bilirubin, and γ -glutamyl transferase (GGT). In a cohort study, (Lin et al., 2017) identified the risk factors for patients of untreated hyperthyroidism and thyrotoxicosis who develop abnormal serum liver function tests (AST, ALT, ALP, GGT, total bilirubin and conjugated bilirubin). (Wafa, Faten, Mouna, Fatma, &

Mohamed, 2020) concluded that liver injury in hyperthyroidism is relatively common ranging from mild to severe, and the patients presenting unexplained hepatic abnormalities require a close examination and evaluation of thyroid function. (Wang et al., 2021) showed that the prevalence of NAFLD in hyperthyroidism patients was 11.97%, and that the higher free T3 was negatively associated with the liver fat content. In a review study, (Yorke, 2022) mentioned that deranged hepatic marker caused by hyperthyroidism rather than intrinsic liver pathology is common suggesting the role of preexisting liver disease, drugs, associated autoimmune conditions, co-morbid heart failure, and direct hepatocyte injury in liver dysfunction untreated hyperthyroidism patients.

Renal markers

Disorders in thyroid hormones might be altered the renal functions by the local and systemic hemodynamic effects; however, data on these impacts remain low. World, there were little reports about the impact of thyroid status on metabolism of BUN which being usually contradictory and/or inconclusive. In this study, our findings reported that the levels of BUN but not creatinine were elevated significantly in thyroidectomy. In an experimental study, authors were found a significant association between thyroidectomy and increases in values of BUN (Keçeci and Kocabatmaz, 1994). In other studies, researchers recorded that one of the important and mostly overlooked manifestations of hypothyroidism is the impairment of renal function since there is an increase in serum creatinine and uric acids with decreasing the glomerular filtration rate (GFR) and renal blood flow rate; however, normal concentration of BUN was seen (Chaudhury et al., 2013; Mooraki, Broumand, Neekdoost, Amirmokri, & Bastani, 2003). Observation of (Hekimsoy & Kavalali Oktem, 2005) in patients with clinical and subclinical conditions of hypothyroidism was significant elevation in serum creatinine levels. (Meenakshi, 2016) concluded that the thyroid hormones have profuse effect on the renal system; however, the levels of creatinine and BUN were differed insignificantly. On the other hand, (Grøfte et al., 1997) revealed experimentally that the moderate hyperthyroidism reduces the overall nitrogen balance; whereas, (Shamsadini, Darvish, Abdollahi, Fekri, & Ebrahimi, 2006) suggested the feedback relationship exists between the major and catabolic products (BUN and creatinine) and thyroid hormone serum level. (Sönmez et al., 2019) study the effects of hyperthyroidism on renal function and found a significant increasing in BUN and creatinine with significant decreasing in GFR.

CONCLUSION

The variable values of liver and kidney enzymes might indicate the alternative association of hyperthyroidism status prior to the surgery and / or the hypothyroidism effect after it. Thus, this study recommends that liver and kidney tests must be evaluated in individuals of thyroid dysfunction. Also, we suggested that various endogenous proteolysis might be related with thyroidectomy due to changes in levels of thyroid hormones (hypothyroidism or hyperthyroidism).

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Conflict of interest

None.

Data availability

All obtained data were involved within the manuscript.

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