PHYSIOLOGICAL EVALUATION OF THYROID GLAND HORMONES DISTURBANCES AMONG ACUTE CHOLECYSTITIS PATIENTS

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ABSTRACT:

The current study was designed to investigate the physiological disturbances of thyroid gland hormones in acute cholecystitis patients (AC). Also, evaluation of immunity status represented by thyroid gland autoantibodies such as, thyroglobulin antibody (TgAb) for both study samples which include (150 participants) male and female including four ages groups (≤ 30, 31-45, 46-60, and ≥ 60 years) and divided into two groups: the first was the control groups of the healthy (50 participants) without acute cholecystitis and the second was the groups of (AC) patients including (100 participants). The demographic data were collected for both patients and healthy groups according to age and ABO-Rh blood groups. Also, the laboratory tests were performed for all venous blood samples taken from both study subjects, including measurements the hormonal activity of thyroid gland such as total triiodothyronine (T3), total thyroxine (T4), and thyrotropin (TSH)). As well as, measurement the levels of thyroid gland autoantibodies such as thyroglobulin antibody (TgAb). The demographical study revealed that the incidence of (AC) infection more occurs in female than male within mid ages (31-45 and 46-60 year). In addition, the predominant blood type among (AC) patients was (O+) followed by (A+) > (B+) > (AB+) > (B- and O-) > (AB-) > (A-). On the other hand, the serum biochemical assay for (AC) patients indicated for significantly decreased in (T3 and T4) concentrations in female patients subjects. While, significantly increased were recorded in (T3 and T4) concentrations in male patients without female within mid age range (46-60 years) in compression with control volunteers. Besides, significant increased were recorded in the levels of thyroid gland autoantibodies (TgAb) in compression with control subjects. It was concluded that the thyroid autoantibodies activity was one of the most common causes for hormonal disturbances of thyroid gland which may be an important risk for gallstone formation and then acute cholecystitis infection.

I. INTRODUCTION:

Acute cholecystitis (AC) is an acute inflammation of the gallbladder, it is the most common cause of acute pain in the right upper quadrant. It is a clinical problem representing up to 5% of emergency room visits (Alghamdi et al., 2018). (AC) may be managed either medically or surgically with a laparoscopic cholecystectomy (removal of the gallbladder and its contents) being the most common operation used for treatment (Gurusamy and Davidson, 2014). The key element in the pathogenesis of acute calculus cholecystitis seems to be an obstruction of the cystic duct in the presence of bile supersaturated with cholesterol. Brief impaction may cause pain only, whereas prolonged impaction can result in inflammation. With inflammation, the gallbladder becomes enlarged, tense, and also wall thickening (Strasberg, 2018). Diets high in refined carbohydrates, high in fat, and low in fiber are associated with increase risk of gallstone formation, physical inactivity too is associated with gallstone disease (Satu, 2016).

However, thyroid release two hormones, thyroxine (T4, tetraiodothyronine) and (T3, triiodothyronine ), these hormones are synthesized in the thyroid gland by iodination and coupling of two molecules of the amino acid tyrosine, a process that is dependent on an adequate supply of iodide (Rousset and Dunn, 2004). On the other hand, thyroid gland is controlled by feedback mechanism system which consist of (hypothalamus, pituitary gland, and thyroid gland). The hypothalamus is responsible for producing thyrotropin releasing hormone (TRH), which is secreted into the venous blood system that drains to the pituitary gland. (TRH) binds to pituitary gland receptors causing production and secretion of thyroid stimulating hormone (TSH). Thyroid stimulating hormone binds
to (TSH) receptors in the follicular cells of the thyroid gland causing production and secretion of thyroid gland hormones, T3 and T4 (Clines and Demers, 2010). On the other hand, thyroid gland exhibit both negative and positive feedback, the negative feedback system is predominates. In negative feedback the hormones produced by the thyroid gland negatively feed back to the hypothalamus and pituitary gland to shut off any access production of thyroid hormones. This negative feedback is responsible for maintaining relatively constant levels of circulating thyroid hormones (Bertholf, 2011). There are several explanations for a possible relation between hypothyroidism and gallstone disease. These explanations include the known link between thyroid failure and disturbances of lipid metabolism that may consecutively lead to a change of the composition of the bile (Völzke et al., 2005). The composition and transport of lipoproteins can be affected in thyroid disease. Hypothyroidism is associated with hypercholesterolemia causing increased concentrations of total and low-density lipoprotein (LDL) cholesterol. While, hyperthyroidism is associated with lower total, (LDL), and high-density lipoprotein (HDL) cholesterol levels and promotion of the reverse cholesterol transport pathway (Wang et al., 2016).

II. MATERIALS AND METHODS

The cases for this study were collected from the patients with a diagnosis of acute cholecystitis before admitted for surgical treatment (laparoscopic cholecystectomy) at the department of general surgery in AL- Karama and AL-Helal hospital of Wasit health directorate in AL-Kut city, Wasit province, Iraq; during the period from December 1, 2018 to December, 1, 2019.

- One hundred patients were taken for this study, 24 males (24.00 %) with age (23-65 year) and 76 females (76.00 %) with age (18-80 year).

- fifty of healthy individuals as control group, 20 males (40.00%) with age (25-65 year) and 30 females (60.00%) with age (20-75 year). Who were without acute cholecystitis symptoms, hyperlipidemia, diabetes mellitus, hypertension and other diseases.

The initial diagnosis of acute cholecystitis was made from the detailed history, clinical examination, and analysis of available laboratory data. Detailed history of the cases was taken such as (age, gender, fertility, weight, length, blood groups, habitation and clinical status) for both samples groups. Both patients and healthy individuals were divided into four groups according to their age ranges; The first age range (≤30 year), second age range (31-45 year), third age range (46-60 year), and fourth age range (≥ 60 year) and each group was divided into two subgroups according to their gender (male and female).

Sample collecting

Ten milliliters of venous blood were drawn from control subjects and (AC) patients by using disposable syringe of (10 ml) before admitted for laparoscopic cholecystectomy, the blood sample was put in disposable gel tubes, left at room temperature for (30) minutes for clot formation and then centrifuged for (10) minutes at (3000) run per minute the serum was distributed in to eppendorf tubes and frezone at (-20 °C). The serum biochemical assay were performed by using Huma reader (ELISA) method, according to kit assay Human laboratories, Germany.

Statistical analysis

The results of current study was done by using statistical software package (SPSS 16) and analyzed by using ANOVA (one way analysis). The data were expressed as mean ± standard error of the mean (M±S.E.M.). LSD were used for comparisons between the acute cholecystitis patients and control group. (P≤0.05) was considered to be statistically significant and LSD was considered to be least significant difference.

Results and discussion

As shown in the figure (1), (100) cases diagnosed with gallstone disease suffering from acute cholecystitis who attended for laparoscopic cholecystectomy, abdominal ultrasound was done for all patients, they were between the ages of (18-80) years. Out of the one hundred cases, twenty four were males (24%) and seventy six were female (76%), the highest percentage of (AC) infection according to gender was recorded in females (76%) than males (24%) patients with (AC). Also, the highest age's percentage among (AC) patients was noted in the second age range (31-45) years (8% males and 28% females), followed by (7%) in males and (18%) females at third age range (46-60) years. While, the lower percentage of (AC) infection were recorded in the late age range (≥ 60) years (4%
males and 12% females). The results of current study indicated that the incidence of (AC) diseases more occur in female than male within mid age ranges.

So, this results agreed with pervious study by Singh et al., (2018) who recorded that (61%) of cholelithiasis patients were (≤ 45) years and females is common in fatty fertile female of forty. Also in same agreement, Khan et al., (2017) who reported that the incidence of gallstones increased in patients were above (35) year of age with increased incidence of gallstone formation in female as compared to male. In contrast, Chauhan et al., (2019) found during a study carried out on (70) patients with cholecystitis in India, no significant differences (P˃0.05) was found between grade of cholecystitis severity and gender as well as age range of cholecystitis patients.

The distribution of percentage of ABO blood groups among (AC) patients are shown in figure (2). The present data showed that the highest percentage among (AC) patients with blood group O+ (39%), followed by A+ (16%), B+ (15%), AB+ (9%), both B- and O- (6%), AB- (5%), and the lowest percentage with A- (4%) . The present phenotypically data showed that the most predominant blood type is (O+) and lowest is (A-) among (AC) patients. Thus, the present results are in line with study done by Alsisi et al., (2019) on patients with cholelithiasis, who found that the majority of the females were suffering from gallstone disease within middle age and the most predominant blood type is (O+) among cholelithiasis patients. Similar finding were reported by Panda et al., (2015) who refer that the incidence of cholecystitis was highest in females and also reported that blood type of (O+) was the highest incidence of the cholecystitis disease among the other blood groups.
Tables (1) and (2) summarizes the results of serum thyroid gland hormones (T3) and (T4) in both study groups respectively, in the first age range (≤ 30 year) our results show no significant differences (P>0.05) in serum (T3) and (T4) for both gender of (AC) patients as compared with control subjects. Where as, in the last age range (≥ 60 year) results indicate clearly significant decrease (p≤0.05) in serum thyroid gland hormones for both gender of (AC) patients in comparison with control participants. Where as, in the last age range (≥ 60 year) results indicate clearly significant decrease (p≤0.05) in serum thyroid gland hormones for both gender of (AC) patients in comparison with control participants. On the other hand, in mid age ranges (31-45 year) and (46-60 year) respectively, our results show highly significant decrease (p<0.05) in serum (T3) and (T4) for both gender of (AC) patients as compared with control participants. In contrast, highly significant increase (p≤0.05) in serum (T3) and (T4) were observed in male (AC) patients in the third age range (46-60 year) as compared with control group. Indeed, the findings based on the age ranges refer to non-significant differences (P>0.05) in both (T3) and (T4) concentration within all age groups (≤ 30, 31-45, 46-60, and ≥ 60 years) in control participants. But, in male (AC) patients serum thyroid hormones were elevated significantly in the third age range in comparison to first, second, and fourth age range. also, in female (AC) patients serum (T3) and (T4) were decreased significantly in the second, third, and fourth age range as compared with first age range.

Thus, cholelithiasis pathogenesis is not unique but appears to be multifactorial (Lambou-Gianoukos and Heller, 2008). It has been shown that disturbances in lipid metabolism that occur during hypothyroidism, particularly cholesterol pathway, changes the rate of bile excretion and lead to the formation of gallstones. Recently, the effect of serum total thyroxin (T4) on both human and pig sphincter of oddi (SO) has been proven. Possibly, the lack of T4 may contribute to (SO) contractility which in turn not only disturbs the normal bile flow but also prohibits the passage of stones formed in the gallbladder to the duodenum. Some researchers have reported a higher prevalence of both hypothyroidism and subclinical hypothyroidism in common bile duct (CBD) stones which supports a possible relation between low (T4) levels and (CBD) stones (Ajdarkosh et al., 2013). Similar suggestions have been reported by Arora, (2017) who observed that there was more prevalence of hypothyroidism in female patients with gallstone disease. Where as, a study conducted by Singh et al., (2016) demonstrated the percentage of males with gallstone disease diagnosed as hypothyroid, euthyroid and hyperthyroid is 24%, 64% and12% respectively.

Table (1): The mean values of serum triiodothyronine (T3) concentration (ng/ml) of acute cholecystitis patients and control subjects according to age range for both genders.

<table>
<thead>
<tr>
<th>Age range (Year)</th>
<th>Control</th>
<th>(AC) Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Male</td>
<td>Female</td>
</tr>
<tr>
<td></td>
<td>Male</td>
<td>Female</td>
</tr>
<tr>
<td>≤ 30</td>
<td>1.265±0.131 Aa</td>
<td>1.316±0.148 Aa</td>
</tr>
<tr>
<td>31-45</td>
<td>1.179±0.192 Aa</td>
<td>1.240±0.107 Aa</td>
</tr>
<tr>
<td>46-60</td>
<td>1.215±0.120 Aa</td>
<td>1.297±0.131 Aa</td>
</tr>
<tr>
<td>≥ 60</td>
<td>1.677±0.212 Aa</td>
<td>1.802±0.102 Aa</td>
</tr>
</tbody>
</table>

LSD= 0.288

Data= Mean ± S. E. M.

Different capital letters denote to significant differences between groups (P≤0.05).

Different small letters denote to significant differences within groups (P≤0.05).

Similar capital and small letters denote to non-significant differences (P>0.05).

LSD = Least significant difference

Table (2): The mean values of serum thyroxin (T4) concentration (mg/dl) of acute cholecystitis patients and control subjects according to age range for both genders.
Data = Mean ± S. E. M.

Different capital letters denote to significant differences between groups (P≤0.05).

Different small letters denote to significant differences within groups (P≤0.05).

Similar capital and small letters denote to non-significant differences (P>0.05).

LSD = Least significant difference.

Tables (3) illustrate the mean values of serum thyroid stimulating hormone (TSH) for (AC) patients and control participants, serum (TSH) levels exhibit no significant differences (P>0.05) in the first age range (≤ 30 year) for both gender of (AC) patients as compared with control subject. While, in the last age range (≥ 60 year) the results indicate clearly significant increase (p≤0.05) for both gender of (AC) patients in comparison with control subject. On the other hand, in mid age ranges (31-45 year) and (46-60 year) respectively, the results show highly significant increase (p≤0.05) in serum (TSH) of female (AC) patients as compared with control group. In contrast, highly significant decrease (p≤0.05) were observed in male (AC) patients in the third age range in compression to first and last age range. Also, in female (AC) patients serum (TSH) were increase significantly (p≤0.05) in second, third, and fourth age range as compared with first age range.

Table (3): The mean values of serum thyroid stimulating hormone (TSH) concentration (IU/l) of acute cholecystitis patient and control subjects according to age range for both genders.

| Age range (Year) | Control | | | (AC) Patients | | |
|------------------|---------|---------|---------|----------------|---------|
|                  | Male    | Female  | Male    | Female         |         |
| ≤ 30             | 7.621±0.490 Aa | 7.760±0.496 Aa | 8.023±0.552 Aa | 7.721±0.281 Aa |
| 31-45            | 7.922±0.684 Aa | 8.199±0.506 Aa | 7.678±0.639 Aa | 3.669±0.270 Bb |
| 46-60            | 8.097±0.529 Aa | 7.235±0.492 Aa | 11.587+2.947 Bb | 3.116±0.275 Cb |
| ≥ 60             | 8.032±0.580 Aa | 7.485±0.342 Aa | 2.340±0.297 Bc | 3.220±0.356 Bb |

LSD = 1.254

| Thyroid stimulating hormone (TSH) (IU/l) | Control | | | (AC) Patients | | |
|----------------------------------------|---------|---------|---------|----------------|---------|
|                                        | Male    | Female  | Male    | Female         |         |
| ≤ 30                                   | 2.920±0.584 Aa | 3.206±0.566 Aa | 2.935±0.372 Aa | 2.623±0.208 Aa |
| 31-45                                  | 3.183±0.496 Aa | 3.245±0.325 Aa | 1.930±0.419 Ab | 7.059±0.499 Bb |
| 46-60                                  | 2.728±0.558 Aa | 2.739±0.330 Aa | 0.223±0.143 Bb | 5.684±0.381 Cc |
| ≥ 60                                   | 3.646±0.448 Aa | 2.703±0.776 Aa | 6.655+1.120 Bc | 5.571+0.593 Bc |

LSD = 1.011
In fact, subclinical hypothyroidism is identified when serum thyroid hormones are within normal lab level, but serum thyroid stimulating hormone (TSH) level is slightly raised (Fatourechi, 2009). There are several explanations for a possible relation between hypothyroidism and gallstone disease, these explanations include the known link between thyroid failure and disturbances of lipid metabolism that may consecutively lead to change of composition of the bile (Hassan, 2018). On the other hand, hyperthyroidism is associated with lower total low density lipoprotein (LDL), and high-density lipoprotein (HDL) cholesterol levels and promotion of the reverse cholesterol transport (RCT) pathway (Pedrelli et al., 2010). So, data in current study was identical to previous studies such as study complemented by jabini et al., (2020) who concluded that hyperthyroidism was prevalent in patients with gallbladder stone. As well as, Ghadhban and Abid, (2019) they proved that statistically significant decrease (p≤0.05) in thyroid hormones in patients with gallstone disease. In contrast, the present data was in disagreement with result of Watali et al., (2017) who refers to no significant relationship between gallstones and hypothyroidism in patient suffering from gallbladder diseases.

Tables (4) illustrate the mean values of serum thyroglobulin antibody (TgAb) for (AC) patients and control participants. The data of the present study investigate to no significant differences (P>0.05) in serum (TgAb ) (IU/ml) level for both gender of (AC) patients in the first and second age ranges (≤ 30, 31-45 year) as compared with control volunteers. Where as, the results an indicate clearly significant increase (p≤0.05) for both gender of (AC) patients in the third and fourth age ranges (46-60, ≥ 60 year) in comparison with control groups. On the other hand, the data based on the age ranges have been shown clearly significant increase (p≤0.05) in serum (TgAb ) (IU/ml) level for both gender of (AC) patients in the third and fourth age ranges (46-60, and ≥ 60 years) as compared with first and second age ranges (≤ 30, 31-45 years). In contrast, the results show no significant differences (P>0.05) in serum (TgAb) (IU/ml) concentration within all age groups among control participants. This study came somewhat identical to the study by Prpic et al., (2018) who referred that the thyroglobulin (Tg) was a primary biochemical tumor marker for patients with differentiated thyroid cancer. Similarly, Lewińska and Bilska, (2012) who concluded that oxidative stress damage in the thyroid gland occur in response to different exogenous prooxidants and this oxidative damage responsible for developing of different thyroid gland diseases. Moreover, the highly production of antibodies against (Tg) can be induced by massive destruction of the thyroid gland, antibodies against (Tg) differ between healthy subjects and (AITD) patients in that polyclonal antibodies are seen in normal subjects and oligoclonal antibodies in (AITD) patients(Marcocci and Marino, 2005).Macdonald et al., (2017) reported that autoimmune thyroid disease is the most common form of thyroid dysfunction causing several forms of thyroiditis ranging from hypothyroidism (Hashimoto’s thyroiditis) and hyperthyroidism (Graves’s Disease).

Table (4): The mean values of serum thyroglobulin antibody (TgAb ) concentration (IU/ml) of acute cholecystitis patients and control subjects according to age ranges for both genders.

<table>
<thead>
<tr>
<th>Thyroglobulin antibody (TgAb ) (IU/ml)</th>
<th>Control</th>
<th>(AC) Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age ranges (year)</td>
<td>Male</td>
<td>Female</td>
</tr>
<tr>
<td>≤ 30</td>
<td>0.551± 0.057 Aa</td>
<td>0.509± 0.040 Aa</td>
</tr>
<tr>
<td>31-45</td>
<td>0.510± 0.077 Aa</td>
<td>0.560± 0.049 Aa</td>
</tr>
<tr>
<td>46-60</td>
<td>0.506± 0.055 Aa</td>
<td>0.522± 0.045 Aa</td>
</tr>
<tr>
<td>≥ 60</td>
<td>0.525± 0.057 Aa</td>
<td>0.570± 0.044 Aa</td>
</tr>
<tr>
<td>LSD= 0.175</td>
<td></td>
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</tbody>
</table>

Data= Mean ± S. E. M.
Different capital letters denote to significant differences between groups (P≤0.05).
Different small letters denote to significant differences within groups (P≤0.05).
Similar capital and small letters denote to non-significant differences (P>0.05).

LSD = Least significant difference.

REFERENCES:


