LIPID PROFILE IN SUBCLINICAL HYPOTHYROIDISM: A TWO CENTERS EXPERIENCE

BAYAR AHMED QASIM, MBChB, MRCP, FKBMS, Endo Diploma (UK)*
AYAD AHMAD MOHAMMED, MBChB, FIBMS**
MAZYAR JABBAR AHMED, MBChB, FIBMS ***

Submitted 05/12/2018; accepted 02/03/2019

ABSTRACT

Background: Subclinical hypothyroidism (SCH) is estimated to affect around 7.5-8.5% of females and 2.8-4.4% of males. One of the features of clinical hypothyroidism is dyslipidemia. There is a great debate about the presence of abnormal lipid profiles in patients with subclinical hypothyroidism (SCH) and whether it is clinically significant or not. Some evidences show reduction in the level of the serum lipid profile after replacement with thyroid hormones. The purpose of this study is to estimate the prevalence of dyslipidemia in patients with subclinical hypothyroidism in Duhok and Erbil cities, Iraq.

Patients and Methods: This is a case-control study that was done on 200 individuals. One hundred patients confirmed with subclinical hypothyroidism were compared with a group of 100 apparently healthy individuals. These two groups were matched for age and sex. The study done in 2 centres; Azadi Teaching Hospital in Duhok and Rizgari Teaching Hospital in Erbil, Kurdistan Region, Iraq from from 1st December 2017 to 1st December 2018.

Results: Dyslipidemia was commoner in patients with subclinical hypothyroidism compared to control group (p value 0.001) compared to the control group (p value 0.766). The total cholesterol and the triglyceride levels were steadily increased in relation to the level of the thyroid stimulating hormone (TSH).

Conclusions: Subclinical hypothyroidism (SCH) is regarded as an atherogenic condition because it increases the cholesterol and the triglyceride levels. Management of subclinical hypothyroidism with thyroid hormones may have a positive impact on the cardiovascular health. It is reasonable to measure the levels of the serum lipids and cardiovascular risk in these patients and to manage them when it is clinically applicable.

Keywords: Dyslipidemia, Subclinical Hypothyroidism (SCH), Case Control Study.

The thyroid gland abnormalities may be seen at any age. They are more common in adults. Thyroid hormones act in the metabolism in all body systems. Their most clear and well known function is to enhance the body energy production which is caused by acting on the metabolism of the fat, the carbohydrates and the protein. The fat metabolism is more affected. Thyroid hormones are important to maintain the phospholipids in cell membranes and fatty acids contents of the lipids. Tri-iodothyronine (T3) plays an important function in fat metabolism.

* Lecturer, Department of Medicine, College of Medicine, University of Duhok, Kurdistan Region, Iraq.
** Lecturer, Department of Surgery, College of Medicine, University of Duhok, Kurdistan Region, Iraq.
*** Physician, Kurdistan Board for Medical Specialities , Kurdistan Region, Iraq.

Correspondence author to: Bayar Ahmed Qasim, Bayarsabc@gmail.com, Mobil +9647507599548
because it regulates the expression of
different genes which control fat synthesis
and catabolism\textsuperscript{1,2}.
Hypothyroidism is caused by decrease
excretion of thyroxin (T4) and T3. Biochemical reduction in T4 and T3 levels
will lead to elevation in the serum thyroid
stimulating hormone (TSH) level. In
clinical hypothyroidism there is high
cholesterol levels in the serum and a
marked increase in low density lipoprotein
(LDL) due to reduction in the catabolism
of LDL by decreasing the number of LDL
receptors in the hepatocytes. However,
debate is present concerning the fat levels
in Subclinical hypothyroidism (SCH) and
its importance clinically\textsuperscript{3,4}.
Non-symptomatic individuals having
elevated thyroid stimulating hormone level
with the presence of normal freeT4 levels
are called subclinical hypothyroidism.
Subclinical hypothyroidism may be
changed to overt hypothyroidism in many
patients. Patients of SCH are usually non-
symptomatic or complain from minimum
symptoms. For this reason, SCH is only a
diagnosed by investigations\textsuperscript{5}.
Clinical thyroid abnormalities may be
suspected due to the presence of thyroid
enlargement. This condition is common
and may be seen in 6-17\% of the people\textsuperscript{6,7}.
The presence of SCH is commoner in
females more than in males and is
estimated to be two times more common.
All over the world around 7.5-8.5\% of
women and 2.8-4.4\% of men have SCH.
The diagnosis depends on the biochemical
analysis which is performed using the
chemiluminiscence technique. The normal
serum TSH level is 0.4 – 4.5 m IU /L.
SCH is one of the causes for coronary
artery diseases, fat derangement, and
congestive heart failure.
The causes of coronary artery diseases are
classified to non-modifiable risk factors
such as age, sex, ethnicity, heredity or
family history and modifiable risk factors
such as hypertension, hyperglycemia, atrial
fibrillation, dyslipidemia, abdominal
obesity, smoking, lack of exercise, alcohol
consumption. Dyslipidemia is among the
modifiable cardiovascular risks because it
is associated with diastolic dysfunction,
abnormal function of the endothelial cells,
decreased elasticity of the arteries,
coagulation pathways and increase the C-
reactive protein (CRP)\textsuperscript{8,9}.
The cause of this fat-level derangements in
patients with clinical and subclinical
hypothyroidism involves increase in blood
cholesterol level which in turn are caused
by alterations in the formation, catabolism,
mobilization of fat in hepatocytes and
adipocytes. Elevated TSH stimulates the
hepatocytes to express hydroxyl-
methylglutaryl coenzyme-A-reductase,
which causes enhancement in cholesterol
formation. In patients with hypothyroidism
the most prevalent lipid profile
derangement is hypercholesterolemia.
Elevated level of the very low density
lipoprotein (VLDL) and the high density
lipoprotein (HDL) is also seen. The
triglyceride level is elevated due to an
enhancement of the esterification of
various types of fatty acids at the
hepatocytes\textsuperscript{10}.
In a new population-based study
subclinical hypothyroidism appears to be
an independent risk for the development of
atherosclerosis of the aorta and ischemic
heart diseases. Peri-menopausal women
tend to have similar symptoms to
hypothyroidism, so evaluation of thyroid hormones in such group of patients may diagnose subclinical hypothyroidism which may be missed easily\textsuperscript{11,12}. Moreover, subclinical hypothyroidism may change to clinical hypothyroidism. The rate of progression is higher with the simultaneous presence of thyroid peroxidase antibodies or increase levels of TSH. Administration of a low dose of thyroid hormones cause a significant reduction in the level of the total cholesterol, non-HDL, LDL, and LDL to HDL values. Recent clinical evidence also shows that treatment with T4 therapy may improve lipid profile in the cases of subclinical hypothyroidism\textsuperscript{13}.

**MATERIALS AND METHODS**

A total number of 200 individuals were included in this study, 100 patients diagnosed with subclinical hypothyroidism with 100 apparently healthy individuals as a control group (matched for age and gender), from 1st December 2017 to 1st December 2018. This study was done in the endocrine clinic at Azadi General Teaching Hospital in Duhok city and Rizgary Teaching Hospital in Erbil city. An informed consent was obtained from patients after explaining the study project. The detailed history was taken and the clinical examination was done for each patient. Each patient was given a special questionnaire to obtain information.

**Inclusion and Exclusion Criteria**

Inclusion criteria include patients having subclinical hypothyroidism, when TSH is greater than 5.0 m IU/L and the free-T3, the free-T4 are below the reference range which was done two times at six weeks in between each test result. Exclusion criteria include patients that have factors that alter thyroid function test such as pregnancy, oral contraceptive pills especially that contain only estrogen, steroids, amiodarone, and phenytoin, liver and kidney diseases, positive personal or family history of thyroid abnormalities, smokers, history of a recent surgical intervention and history of acute illness such as critical illness which causes abnormalities in thyroid hormone levels. Also Patients taking medications that lower the lipid levels have been excluded. In older patients, higher TSH (>6) used to diagnose subclinical hypothyroidism, patients more than 65 years of age have been excluded\textsuperscript{14,15}.

**Definition of Dyslipidemia**

Dyslipidemia cut-point is based on the AACE guideline, this include; a total cholesterol desirable less than 200 mg/dl, borderline level high between 200- 239, high level greater than 239 mg/dl. HDL cholesterol: dyslipidemic lower than 40 mg/dl in men and lower than 50 mg/dl in women. LDL cholesterol: Optimal lower than 100 mg/dl, near-optimal between 100–129 mg/dl, borderline high between 130-159 mg/dl, high between 160 -189 mg/dl, very high if greater than 189 mg/dl. The triglycerides level: Normal if less than 150 mg/dl, high if between 150-199 mg/dl, Hypertriglyceridemia when the levels are between 200-499 mg/dl, very high if greater than 499 mg/dl\textsuperscript{16}.

**STATISTICAL METHODS**

Statistical analyses were done using the Statistical Package for Social Science (SPSS); \( p \) values less than 0.05 were considered significant.
LIPID PROFILE IN SUBCLINICAL HYPOTHYROIDISM: A TWO CENTERS

RESULTS
The majority of the patients in the study were between 40-50 years (53%) while 26% of the patients were between 50-60 years. Female patients constitute 53 % of the involved participants. The relation between the level of the TSH and the data taken from the patients showed a significant relation with the dyslipidemia (p value 0.001) and with the HDL (p value 0.002), while no factor had been found to be related to the TSH level in the control group. Other factors and their relation to the TSH are shown in Tables 1 and 2.

<table>
<thead>
<tr>
<th>Table 1: Relation of TSH Level and the Lipid Profile with the Patients Factors in the Patients Group.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dependent factor: TSH level for patients group</td>
</tr>
<tr>
<td>Standardized Coefficients</td>
</tr>
<tr>
<td>---------------------------</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Age</td>
</tr>
<tr>
<td>gender</td>
</tr>
<tr>
<td>Dyslipidemia</td>
</tr>
<tr>
<td>Total cholesterol</td>
</tr>
<tr>
<td>LDL</td>
</tr>
<tr>
<td>TG</td>
</tr>
<tr>
<td>HDL</td>
</tr>
<tr>
<td>Comorbidities</td>
</tr>
</tbody>
</table>

| Abbreviations: LDL: low density lipoprotein, TG: triglycerides, HDL: high density lipoprotein. |
| The bold number show the predictors |

<table>
<thead>
<tr>
<th>Table 2: Relation of the TSH Level and the Lipid Profile with the Control Group.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dependent factor: TSH level for control group</td>
</tr>
<tr>
<td>Standardized Coefficients</td>
</tr>
<tr>
<td>---------------------------</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Age</td>
</tr>
<tr>
<td>Gender</td>
</tr>
<tr>
<td>Dyslipidemia</td>
</tr>
<tr>
<td>Total cholesterol</td>
</tr>
<tr>
<td>LDL</td>
</tr>
<tr>
<td>TG</td>
</tr>
<tr>
<td>HDL</td>
</tr>
</tbody>
</table>

The relation between the dyslipidemia and the TSH levels is shown in Figure 1, the level of the abnormal lipid profile is significantly high in patients in whom the TSH levels are higher than 5.
The cholesterol and the triglycerides levels tend to be significantly higher in patients with TSH levels higher than 5, Figures 2 and 3.

Figure 1: The Relation between the Presence or the Absence of Dyslipidemia and the TSH Level.

Figure 2: The Relation between the Cholesterol Level and the TSH Level.

Figure 2: The Relation between the Triglycerides Level and the TSH Level.
LIPID PROFILE IN SUBCLINICAL HYPOTHYROIDISM: A TWO CENTERS

DISCUSSION

The presence of SCH increases the risk of development of the clinical hypothyroidism, lipid level derangement, and major cardiac and vascular risk, which include diastolic impairment, coronary artery diseases, cardiac failure and increase in morbidity and death rate. However, SCH may be temporary and improvement may occur with time that is why finding cases, who need management, is a difficult in medical practice. Many authors discovered direct correlation of this abnormality and the development of coronary artery diseases. The presence of abnormal lipid profiles may explain the increased coronary artery events in this population of people because it is direct cause of atherosclerosis. However, numerous articles mention that such relation don’t exist. Data from our patients shows a very strong correlation between subclinical hypothyroidism and abnormal lipid profiles as it is found to be commoner in patients with SCH in when compared to the control group (p value 0.001 and 0.766) respectively, and this has the same clinical evidence comparing to the findings of numerous other studies worldwide, which also show similar correlation as in our study.

Further interpretation of dyslipidemic patients; i.e., the cholesterol level and triglycerides level showed a significant increase in their levels when the level of the TSH also get higher. This in accordance to many other studies done in some parts of the globe. LDL level was greater in the patient group when compared to the control group. This relation is found to be statistically not so significant if its compared to the levels of the HDL which also showed a statistically significant value in the patients group (p value of 0.002) but there was no correlation with any of these in the control group. This statistical differences may reflection the pattern of dyslipidemia in the populations of this region and larger population based studies needed to prove or exclude this.

Furthermore, evidence emerges that management with thyroid hormones decrease serum lipid levels in patients having SCH which may decrease the morbidities and the mortality from the cardiovascular events, for this reason it is very important to manage patients having SCH and dyslipidemia properly. Even a mild decrease in the cholesterol level of, triglycerides and the LDL may significantly decrease in the cardiac and the vascular morbidity in the future. Subclinical hypothyroidism is found to be an atherogenic status as it causes dyslipidemia and it enhances the cardiac and the vascular risk. Management of patients having subclinical hypothyroidism with thyroid hormones improves the quality of life and deaths from coronary vascular diseases. It’s reasonable to measure the lipid profiles and cardiovascular risk factors in such patients and to manage them with thyroid hormones when it can be applied in clinical practice.

REFERENCES

1. Axelband F, Dias J, Ferrao F, Einicker-Lamas M. Nongenomic signaling pathways triggered by thyroid hormones and their metabolite 3-iodothyronamine on the

https://doi.org/10.31386/dmj.2019.13.1.6

2. Mariela JC, Yamila VC, Liliana BO, Maria SG. Hypothyroidism on Lipid Metabolism, Hypothyroidism - Influences and Treatments: Drahomira Springer; February 8th 2012.


5. Surks MI, Ortiz E, Daniels GH, Sawin CT, Col NF, Cobin RH, et al. Subclinical thyroid disease: scientific review and guidelines for diagnosis and management. Jama. 2004;291(2):228-38.


پوخته

طهرینه ل شیوی ضاروریان ناظ خویینی دا یا دیار بینتاقبی: ظاکولینا لیزانینی یا دو ستانترین جودا

پیشنهدی: روششن کیم و کوری یا سایروده رذینا ذیر بینتاقبی دهیت دانان کو کارتیکرنه ل تا 7.5 تا 8.5 % د مینیا و 2.8 تا 4.4% ذ نیریان دکتک. نیک د سیافتین ظی کیم و سیارتی کیمیکه و طهرینه ل شیوی ضاروریان ناظ خویینی دیه، هتروفسا طفتوپیکا ماتن هایه سخبارت ظان طهرینا نتیج میکشکنه یا بینتاقبی هایه یان نه. هندوک جاران ناظ کیبیرونه لنستی شیوی ضاروری دا دیار دکتک شستی طهرینکنه هرمونین سایروده رذیندا.

نرمانج: نارمانج نئی ظاکولینی تیبته هستن و ریزا پترالاطوبونا طهرینا شیوی ضاروریان ناف خویینی دا. بو وان ناخوشین کیم و کوری یا سایروده رذینا دیار بینتاقبی هایی ل هاتردو بانیرین دهک و هاتویکر عراقی.

ریکین ظاکولینی: ناظ ظاکولینا روش و پالتقا لستر 200 کمسن هایه کرن، هتروفسا دی بتراورديدن ناظبریا 100 کمسن توشبیوی ب کیم و کوری یا سایروده رذینا ذیر بینتاقبی دی پالتقا 100 کمسن روشنا وان یا کلسینیکا دا دیابی بیت هتروفسا دی وردکاری هایه کرن یا هاتردو طروثان ذ لایی یی و رفتهی. ناظ ظاکولینی هایه کرن ذ لایی دوو ستانترین جودا ل ناخوشمان نازاگی یا فیرکره لریووکه و ناخوشمان رازطری یا فیرکره لهاتویکر، هراتیم کوردستانی عراقی د 1 کانینا نئیک 2017 دا کو 1 کانینا نئیکی 2018.

ناخندیام: روششن کیمیکه و طهرینه ل شیوی ضاروریان ناف خویینی دا بالاطر بو د دفع ناخوشین کیم و کوری یا سایروده رذینا ذیر بینتاقبی هایی (ریزا ناظتره 0.000) بتراوردکری دی پالتقا طرثی کورنولوکره (ریزا ناظتره 0.766). ریزا کولیعتریمکه و ضاروریان نستان هایه سخبارت هایه سخبارت دیه طلطل نانستی هرمونین سایروده رذین ل ناظ خویینی دا.
LIPID PROFILE IN SUBCLINICAL HYPOTHYROIDISM: A TWO CENTERS

الخلاصة

واجهة الدهون لدى حالات قصور الغدة الدرقية غير السريرية: دراسة خبرة مركزين مختلفين

الخلفية والأهداف: تقدر حالات قصور الغدة الدرقية غير السريرية بأنها تؤثر على حوالي 7.5-8.5% من الإناث و 2.8-4.4% من الذكور. واحده من سمات قصور الغدة الدرقية غير السريرية هي خلل في واجهة الدهون في الدم، هناك جدل كبير حول وجود خلل في ملامح الدهون و هل أهمية سريرية أم لا. تظهر بعض الأدلة انخفاض في مستوى الملف الدهن في الدم بعد الاستعاضة عن هرمونات الغدة الدرقية. الغرض من هذه الدراسة هو تقدير انتشار خلل في ملامح الدهون في الدم لدى المرضى الذين يعانون من قصور الغدة الدرقية غير السريرية في مدينتي دهوك وأربيل، العراق.

المواضيع و طرق البحث: هذه هي دراسة الحالات والشواهد، التي أقيمت على 200 شخص. سيتم مقارنة 100 مريض من قصور الغدة الدرقية غير السريرية مع مجموعة من 100 شخص طبيعي سريري تتم متابعة هاتين المجموعتين عن العمر والجنس. الدراسة التي أجريت في مركزين مختلفين و هما مستشفى آزادي التعليمي في دهوك ومستشفى ركاري التعليمي أربيل، إقليم كردستان، العراق للفترة من 1 ديسمبر 2017 إلى 1 ديسمبر 2018.

النتائج: كان حالات الخلل في ملامح الدهون في الدم أكثر شيوعا لدى المرضى الذين يعانون من قصور الغدة الدرقية الغير السريرية (القيمة الاحتمالية:0.001) مقارنة مع مجموعة السبطة (القيمة الاحتمالية:0.766). مستوى الكوليسترول الكلي ومستويات الدهون الثلاثية يتناسب بشكل طريدي مع مستويات هرمون الغدة الدرقية في الدم.

الاستنتاجات: يعتبر قصور الغدة الدرقية الغير سريري سببا لحالات تصلب الشرايين لأنها تزيد من مستوى الكوليسترول ومستويات الدهون الثلاثية. علاج حالات قصور الغدة الدرقية الغير السريرية بواسطة هرمونات الغدة الدرقية قد يكون لها تأثير إيجابي على صحة القلب والأوعية الدموية. يجب قياس مستويات الدهون في الدم لتفريق مخاطر القلب والأوعية الدموية لدى هؤلاء المرضى عند تشخيصها سريريا.

https://doi.org/10.31386/dmj.2019.13.1.6 65