Study of the estimation concentration thyroid hormone and lipid profile in overt hypothyroidism patients in Misurata

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ABSTRACT

Background and Aim: Overt hypothyroidism (OH) has been found to be a pathogenic relationship with dyslipidaemia, that is leading to risk Cardiovascular Diseases (CVD). The current study aimed to estimation concentration thyroid hormone and lipid profile in overt hypothyroidism patients in Misurata.

Materials and Methods: The data for the present case - control study was carried out on 115 (83patients diagnosed OH and 32 control), aged (20 to above 50 years old), who attended the outpatient and inpatient diabetic and endocrine center in Misrata, from 27th December, 2017 to 21th March 2018. Their blood was collected for determination of Free Tri-iodothyronine (FT3), Free Tetra- iodothroxine (FT4) and Thyroid Stimulating Hormone (TSH) by using**(Elecsys 2010 autoanalyser)**, whereas the lipid profile Total Cholesterol (TC), Triglyceride (TG), High Density Lipoprotein (HDL), Low Density Lipoprotein (LDL) using **(I Lab 300 plus)** Clinical Chemistry System, and Very Low Density Lipoprotein (VLDL) **(formulas Friedewald).** The association was analyzed using SPSS version 19.0 and was expressed as mean ≠ SD by (*T*-test, *U*- test) with ($P \leq 0.05$).

Result: The results of this study showed that OH in the females higher than in the males, level TSH was increased significantly **(P≤ 0.05)**, while the levels FT3 and FT4 were found to be decreased significantly at **(P≤ 0.05)** in patients compared with those of control. The results of this study clarified that levels of TG, VLDL, were only significantly higher **($P \leq 0.05$)** in patients than control, while unsignificant increase in the levels of TC and LDL, and unsignificant decrease in HDL level at ($P > 0.05$) in patients compared to the control.

Conclusion: There was a significantly statistical TST, FT3 FT4, and. some lipid profile, Any alteration of TH causes changes in lipids.

Keywords: Overt hypothyroidism, Subclinical Hypothyroidism, Cardiovascular Diseases, Thyroid hormone.

1. INDRODUCTION

Hypothyroidism can be defined as a clinical syndrome resulting from dysfunction in secretion or loss activity of Thyroid hormone (TH) via thyroid gland, Hypothyroidism is associated with adverse effect on protein, carbohydrate and lipid metabolism. Thus, alterations in carbohydrate, lipid and lipoprotein metabolism, consequently changing the concentration and composition of plasma lipoproteins in hypothyroid patients, TC and LDL is increased. Hypothyroidism can be divided into Subclinical and Overt (Masullo et al, 2018 & Manuchehri, 2008).

OH, it is also known as clinical or primary hypothyroidism (Shashi & Sharma, 2012). is characterized by increased serum TSH levels, despite decreased fT4 and fT3 levels, and also elevated in serum both of TC, TG, LDL and VLDL levels concentration and decreased in serum of HDL level concentration (Duntas, 2002). in addition to decrease serum thyroid hormone levels, is associated with reduced metabolism, reduced lipolysis, increased weight gain, reduced TC clearance, and elevated TC. It is known that TH has genomic and non-genomic effects (Hammes & Davis, 2015). Subclinical hypothyroidism It is known mild hypothyroidism (Saini, 2012) which categorized by slightly elevated serum level TSH concentration, normal serum level both FT3 or T3 and FT4 or T4 concentration (Wanjia et al, 2012).

Cause of the Hypothyroidism can be iodine associated as reported by (Zimmermann, 2009) or diseases associated like Autoimmune lymphocytic thyroiditis, Infiltrative disease, Transient, Neonatal / Hereditary or congenital, Secondary Hypothalamic pituitary disorders, water and food pollution and drug (Yousif, 2001), as a matter of fact, Subclinical is without symptoms on the patient (Saini, 2012). It can also be resulting from Subclinical Hypothyroidism (SCH) in many patients (Aryal & Joshi, 2014).

Materials and Methods

The data for the present case - control study was carried out in 32 of them were euthyroid control among of them (16 males and 16 females) and 83 patients were suffering only from OH for sexes (32 males and 51 females), who attended the outpa-

tient (hospital center Misurata department of internal medicine, Al Salam and Al Hesan clinic) and inpatient of diabetic and endocrine center in Misurata. From 27th December, 2017 to 21st March 2018. Inclusion criteria all the patients having OH and who have been previously diagnosed, with the age of (20 to above 50 years). Exclusion criteria includes a cases family history of hyperlipidemia, patients taking systemic medicine especially lipid - lowering agents such as (phenytoin, dopamine, estrogen pills, steroids, beta-blockers, amiodarone and iodine - containing drugs) for dyslipidemia, pregnant, lactation.

About 10 ml of venous blood sample were collected between (8.00 -10.00 Am) after fasting of 12 - 14 hour by venipuncture from patients and controls, local antiseptic used to clean the arm vein, using a 10 ml disposable syringe and put it in plain tube (without anticoagulation), the blood was allowable to clot in plain tube an hour time at room temperature. The serum was separated from whole blood for all samples by centrifuged at about 3000 revolution for 5 to 10 minutes (Yousif, 2001; Abd AL-fatah, 2008), then serum was separated into two tubes for estimation of TC, TG, HDL-C, LDL, other the tube of TSH, FT3 and FT4.

Statistical analysis

The data collected ware analyzed by using the computer facility of the available statistical software packages of Statistical Package for Social Sciences (SPSS), version 19 was employed for statistical analysis. The normality of the data distribution was tested by the Shapiro- Wilk test; all quantitative data were obtainable as mean ± Standard Deviation (SD). Student `s independent (T-test) and Mann-Whitney (U-test), whichever suitable, was used to compare the constant variables of two groups with other parameters from thyroid hormones and lipid profile where two - sided measured less than or equal to 0.05 ($p \leq 0.05$) for significant differences.

RESULTS

Distribution of study sample according to Gender

It was observed from **Figure** 1**.** That A majority of the patients 44.4 % were females and only the remaining 27.8 % of the patients were males. Control were also chosen accordingly with 13.9 % in the females and the male's groups.

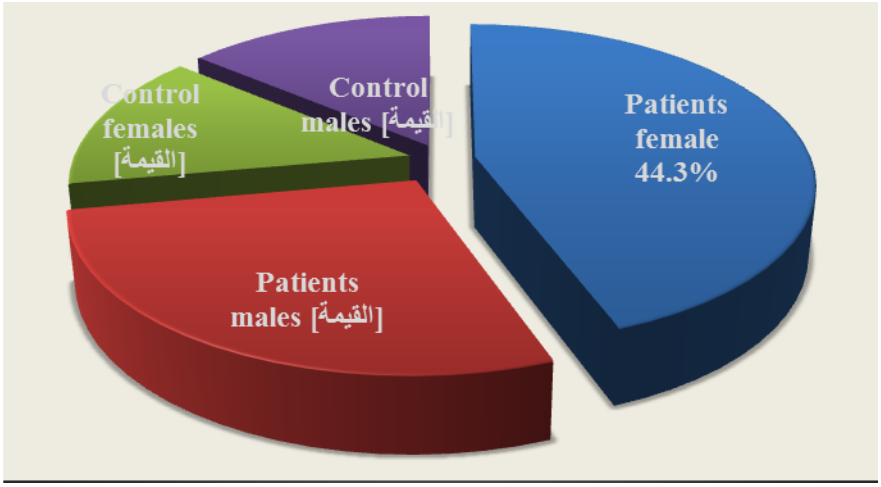

Figure 1 Percentage of both gender Patients and Control

The comparison of Thyroid Hormones among patients and control

According to **Figure 2**, Level TSH significantly higher while levels FT3 and FT4 significantly lower were recorded in patients compared to control, the significance differences seen among levels TSH at (P = 0.015), FT3 at (P = 0.000) and FT4 at (P = 0.029).

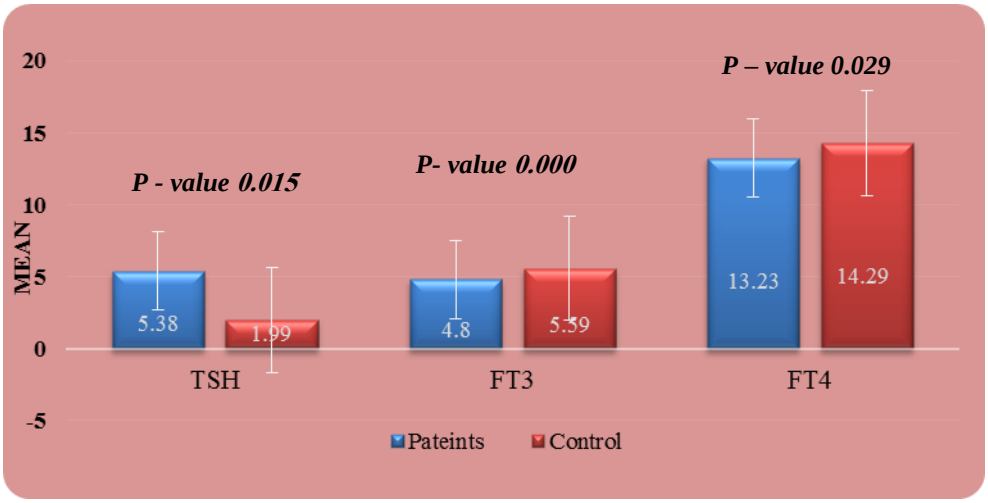

Figure 2 The comparison of Thyroid Hormones among Patients and Control

The comparison of Lipid profile among patients and control

In this study according to the lipid profile in patients and control groups statistical analysis of the results revealed that there were unsignificant differences in the mean of the both TC and LDL among patients and control. The levels TC and LDL were increased in patients, but not a statistically significant at (P = 0.391, P = 0.931 respectively). On the other hand, the level HDL was decreased in patient's comparative to control, and no significant differences at (P = 0.315).

Finally, regarding the levels TG and VLDL results showed that there is a higher significantly differences at (P = 0.008), as seen in **Figure 3**.

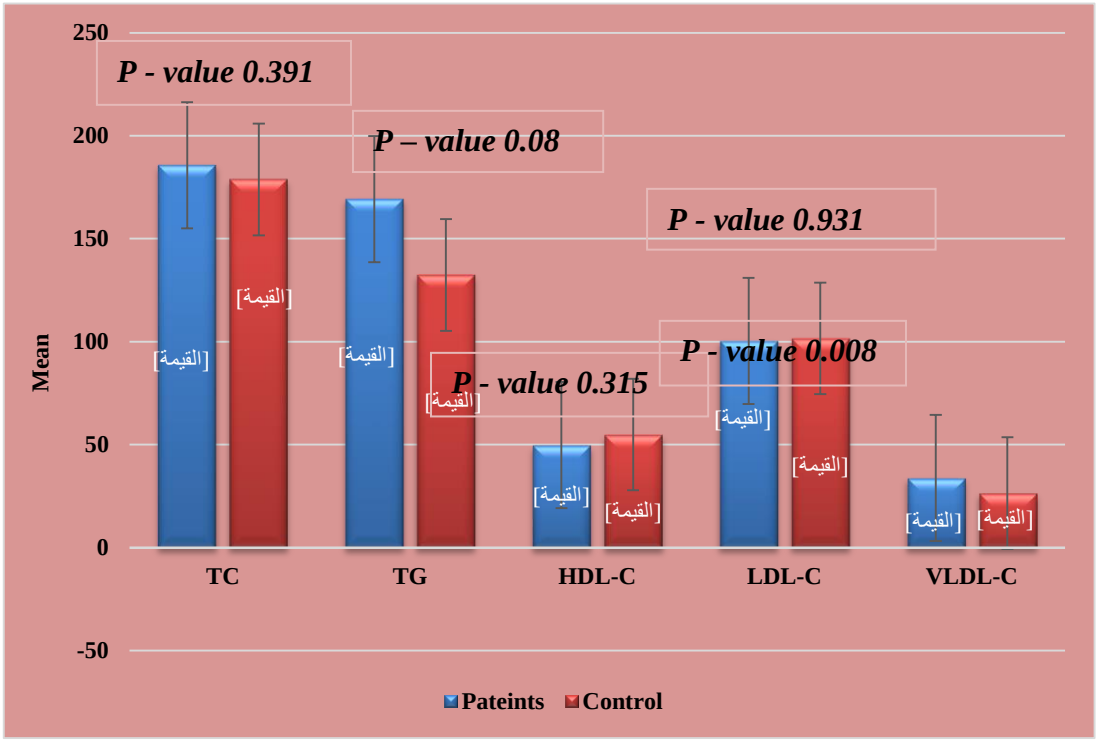

Figure 3 The comparison of Lipid profile among Patients and Control

DISCUSSION

OH, is one of the most common disorders seen in present days especially among females. It causes a derangement of most of the parameters of our body which collectively contributes to the risk of development of Atherosclerotic CVD (Shilpashree., 2012). TH it has a direct effect on basal lipid profile. It is well known that any changes in TH results alterations in the composition lipid profile and the transport of lipoprotein. Thus, this effect on the functions of some important organs such as kidney, liver, muscular- skeletal system, etc.

OH, is one of the main causes of secondary dyslipidemia, as it is correlated with increased lipid profile, which may lead to increased risk of coronary artery disease (Saini et al., 2012). A study by the Mayo Clinic that assessed the lipid profile of 268 SCH and OH patients, dyslipidemia was detected in 91.4% as reported by (Obrien et al, 1993). Various studies support a biologically plausible role for hypothyroidism increasing the risk of atherosclerotic CVD, via altering the lipid profile and making it more atherogenic (Cappola & Ladenson, 2003). In addition, hypothyroidism also increases the oxidation of plasma cholesterol mainly because of (i) an altered pattern of binding and (ii) due to the increased levels of cholesterol, which presents substrate for oxidative stress This further increases the risk of atherosclerosis.

This study has shown the prevalence of OH is highest in the females compared to males. The higher incidence of OH in females were (62.85%) which compared to males were (37.13%) in study done by (Kumari et al, 2017) is consistent with findings in our study in which (44.4%) of the patients are females while males were (27.8%). Accordingly, the analysis showed maximum patients were female and it was about two times compared to the male patients with advanced aged. This is may be due to stress and fatigue, after menopause and beyond. In addition to pregnancy effects on the immunity of females and causing OH.

The result in this study has recorded the agreement with the several studies include (Singh & Sarkar, 2014; Adlat et al, 2016; Malik et al, 2018). Who show that there were highly significant of THS and notable significant of FT3 and FT4 in OH. The abnormal thyroid hormone levels in OH. May be due to the loss of negative inhibition on the anterior pituitary. The levels of serum TSH are considered to be the most important indicator for the evaluation of TH (Castellano et al, 2013). Moreover, the

levels of serum FT3 and FT4 are the active biological in circulation hence, FT3 and FT4 levels are measured to be complex and significant indicators for the analysis of thyroid disease (Li et al, 2014). In accordance to, National Health and Nutrition Examination Survey serum of TSH level increased with age in the sexes (Vanderpump, 2011).

According to the results stated herein a higher level of TC and LDL were found in OH patients than in control in this study and no difference was found to be statistically significant, dyslipidemia was observed among patients. The result of this study disagrees with the studies done by (Sangeeta et al, 2016; Alsalmi et al, 2018) who reported that there is a significant increase of TC and LDL in OH .Also, a Study done by (Jhansi Lakshmi et a l, 2013) shown that hypothyroidism result in a small increase in LDL, that enhance the risk for development of atherosclerosis and coronary artery disease, and other study by (Al-Fartusie et al, 2019) in hypothyroidism, patients with high and low blood pressure. Anther a study done by (Amer & Haridas, 2017) who found that females with OH had significantly higher LDL. The levels of TC and LDL were elevated in patients with OH in this study, decreased thyroid secretion was accompanied by reduced activity of HMG Co - A, thus decreased absorption of TC from intestines led to reduced allowance of concentration TC and LDL from circulation, thus decreased transfer of TC to bile acids in liver (Abrams et al, 1981) and also due to reduces the expression of LDL MRNA and the LDL - cellular receptor numbers and the binding of LDL to LDL receptor, activity of cell surface on the liver that leading to decreased receptor - mediated catabolism of LDL particles and Intermediate Density Lipoprotein (ILD) and increased half-life of LDL, reduced degradation of LDL in the fibroblasts, enhanced residence time in serum, (Thompson et al, 1981), increased fractional catabolic rate of Apo B (Duntas, 2002), increase promotes LDL Oxidability (Costantini et al, 1998) and also Lipoprotein A (LP a) Lives (Tzotzas et al, 2000). Finally, leading to hypercholesterolemia (Zhu & Cheng, 2010). Therefore, increasing CVD risk (Regmi et al, 2010). That could be due to, what is called, Levothyroxine treatment, with different doses for patients that may reduce TC.

Results in this study revealed that a decreased in the level of HDL were found in OH patients than in control, but it is statistically unsignificant, thus the result was

agreed with other studies achieved by (Singh & Sarkar, 2014) that have shown that OH is not associated with a lower HDL. In a report comparing 52 patients with SCH, 56 with OH and 44 with 100 euthyroid control matched for age, sex. Another search done by (Zhenjiang et al, 2017) they reported that there is no significant difference in HDL among 60 patients with SCH and OH and control lower than the control, also by (Obaid, 2019) reported that the decreased HDL in patients with hypothyroidism, compared with control. It has been noticed that the studies done by (Shashi & Sharma, 2012) observed that the HDL a significant decreased in SCH and OH patients in comparison to control, reported (Mathur et al, 2018) there is found significantly lowered HDL in hypothyroidism. in (Adlat et al, 2016) was HDL higher than in hypothyroidism, disagree with the findings of this present study. HDL is mainly secreted by the small intestine and the liver and the body can not completely hydrolysis TC (Huang et al, 2019). Some previous studies in OH increase in levels of HDL concentration is mainly due to increase concentration of HDL2 particles, due to a reduced activity of HL, a decrease catabolism of HDL2 (Lam et al, 1986) and decrease activity of CETP results in reduced transport of CHE from HDL2 to VLDL, resulting in increased HDL (Dullaart et al, 1990). Accordingly, in this study there is decrease in levels of serum HDL and might be a result of increased activity enzymes of CETP, HL, and LPL.

In his study found a significantly increased TG and VLDL in OH than control, obtained among studied groups these results are concurred with other results obtained in other studies such as (Satyanarayana & kumar, 2019) OH patients elevated TG level associated with increased VLDL lives. In recent study (Sharma et al, 2019) on the pattern of dyslipidemia in hypothyroidism higher significant TG and VLDL also support the findings of this study. hence, but not agreed with (Regmi et al, 2010) in levels of serum TG, relatively few studies have been carried out on the alterations of TG and VLDL metabolism in clinical thyroid disease. Typically is in sharp differentiate to the circumstance in TC metabolism, which is well explored in both hyper- and hypothyroidism and is generally believed to undergo typical and consistent changes in both conditions (Nikkila & Kekki, 1972). This attributable to the decline activity of LPL, LPL is a key enzyme in lipid metabolism (Wung et al, 2006) and also observed in OH (Nikkila & Kekki, 1972), which is responsible of the hydrolysis TG from TG rich lipoprotein into VLDL - C and Chylomicrons (CM) into fatty acid

and glycerol (Zhu & cheng, 2010). Thereby, resulting in decreased clearance of TG rich lipoproteins (Nikkila & Kekki, 1972). Thus, reflecting in the decline activity HL enzyme (Shekhar et al, 2011). As a result, increased levels of serum TG correlated with increased levels of serum VLDL -C and occasionally fasting chylomicronemia (Al- Tonsi et al, 2004).

CONCLUSION

In the Misurata City, Libya. Patients with OH in this study were more common among females than males.

In OH was associated with abnormalities in the serum TSH, FT3, FT4, TG, VLDL levels, so any alteration of TH causes changes in some lipid profile. Hence, finally dyslipidemia may be leading to development of CVD atherosclerosis.

References

Abd AL- Fatah, H. S. (2008). Effect of thyroid gland dysfunction on serum leptin and lipid profile in women. (Master dissertation, University of Baghdad), 1-97.

Abrams, J. J., & Grundy, S. M. (1981). Cholesterol metabolism in hypothyroidism and hyperthyroidism in man. Journal of lipid research, 22(2), 323-338.

Adlat, S. A., Shamsan, B., & Al-Eryani, E. (2016). Lipoprotein (a), Lipid Profile and Mean Platelet Volume in Hypothyroid Patients in Sana'a, Yemen: A Case-Control Study. Yemeni Journal for Medical Sciences, 10, 6-14.

Al-Fartusie, F. S., Nabil, N., & Zgeer, D. S. (2019). Evaluation of Lipid Profile and Thyroid Function in Hyper and Hypotensive Patients: A Case Control Study. Indian Journal of Public Health Research & Development, 10(4), 609-614.

Alsalmi, W. M., Shaglouf, L. H. F., & Azab, A. E. (2018). Correlation Between Hypothyroidism, Hyperthyroidism, and Lipid Profile in Thyroid Dysfunction Patients. Clinical Medicine Journal, 4(2), 6-14.

Al-Tonsi, A. A., Abdel-Gayoum, A. A., & Saad, M. (2004). The secondary dyslipidemia and deranged serum phosphate concentration in thyroid disorders. Journal of Experimental and molecular pathology, 76(2), 182-187.

Amer, H. R., & Haridas, N. (2017). Correlation between Thyroid-Stimulating Hormone and Lipid Profile in female patients of clinical and subclinical hypothyroidism. PARIPEX- Indian Journal of Research, 6(9), 1-3.

Aryal, S., & Joshi, A. (2014). Serum Lipid Profile in Hypothyroid Patients in Nepal. Journal of Universal College of Medical Sciences, 2(4), 33-36.

Cappola, A. R., & Ladenson, P. W. (2003). Hypothyroidism and atherosclerosis. The Journal of Clinical Endocrinology & Metabolism, 88(6), 2438-2444.

Castellano, C. A., Laurin, D., Langlois, M. F., Fortier, M., Tessier, D., Gaudreau, P., Ferland G., Payetet, H., Lorrain, D., & Cunnane, S. C. (2013). Thyroid function and cognition in the euthyroid elderly: A case–control study embedded in Quebec longitudinal study–NuAge. Psychoneuroendocrinology, 38(9), 1772-1776.

Costantini, F., Pierdomenico, S. D., Cesare, D. D., De Remigis, P., Bucciarelli, T., Bittolo-Bon, G., Cazzolato, G., Nubile, G., Guagnano, M.T., Sensi, S., & Cuccurullo, F. (1998). Effect of thyroid function on LDL oxidation. Journal of Arteriosclerosis, thrombosis, and vascular biology, 18(5), 732-737.

Dullaart, R. P. F., Hoogenberg, K., Groener, J. E. M., Dikkescheo, L., Erkelens, D. W., & Doorenbos, H. (1990). The activity of cholesteryl ester transfer protein is decreased in hypothyroidism: a possible contribution to alterations in high- density lipoproteins. European journal of clinical investigation, 20(6), 581-587.

Duntas, L., H. (2002). Thyroid disease and lipids. Journal of the American Thyroid, 12(4), 287-293.

Friedewald, W. T., Levy, R. I., & Fredrickson, D. S. (1972). Estimation of the concentration of low-density lipoprotein cholesterol in plasma. without use of the preparative ultracentrifuge. Journal of Clinical chemistry, 18(6), 499-502.

Hammes, S. R., & Davis, P. J. (2015). Overlapping nongenomic and genomic actions of thyroid hormone and steroids. Journal of Best practice & research Clinical endocrinology & metabolism, 29(4), 581-593.

Huang, F., Wu, L., Qiu, Y., Bu, K., Huang, H., & Li, B. (2019). The role of free triiodothyronine in high-density lipoprotein cholesterol metabolism. Medicine, 98(36), 1-5.

Jhansi Lakshmi. L., Eli, M., Doddigarla, Z., & Suchitra, K. (2013). Serum lipid a doxidative stress in hypothyroidism. Journal of Advance Researches in Biological Sciences, 5(1), 63-66.

Kumari, B., Kumar, P., Keshari, J. R., Kumar, A., Pankaj, S., & Chaudhary, R. K. (2017). Serum BUN and creatinine estimation in patients of overt hypothyroidism: a case control study. International Journal of Research in Medical Sciences, 5(9), 3990-3993.

Li, H., Yuan, X., Liu, L., Zhou, J., Li, C., Yang, P., Zhang, M., & Qu, S. (2014). Clinical evaluation of various thyroid hormones on thyroid function. International Journal of Endocrinology, vol 2014, 1-5.

Lam, K. S., Chan, M. K., & Yeung, R. T. (1986). High-density lipoprotein cholesterol, hepatic lipase and lipoprotein lipase activities in thyroid dysfunction—effects of treatment. QJM: An International Journal of Medicine, 59(2), 513-521.

Malik, A., Zaman, A., Izhar, K., & Iqbal, Y. (2018). Correlation of Thyroid Stimulating Hormone with Homocysteine and Lipid Profile in Hypothyroidism. Journal of Liaquat University of Medical & Health Sciences, 17(03), 147-151.

Manuchehri, A. M. (2008). The Impact of Thyroid Dysfunction on Cardiovascular Risk. (Doctoral dissertation, The University of Hull), 1-160.

Masullo, L. F., Magalhaes, R. A., Lemes, R. P. G., de Almeida Filho, T. P., de Castro, M. F., Maia Filho, P. A., Cunha, T. O. V., Quidute, A. R. P., Fontenele, E. G. P., Sun, G., & Martins, M. R. A. (2018). Levothyroxine Replacement Improves Oxidative Status in Primary Hypothyroidism. Journal of frontiers in Endocrinology, 9(655), 1-5.

Mathur, R.D., Gupta, R.P., Gupta, D., Mathur, R., & Bhargav, A. K. (2018). Correlation between association of hypothyroidism and cardiovascular risk indices. International Journal of Advances in Medicine, 5(3), 754-756.

Nikkilä, E. A., & Kekki, M. (1972). Plasma triglyceride metabolism in thyroid disease. The Journal of clinical investigation, 51(8), 2103-2114.

Obaid, M., Ashraf, M., Majid, S., & Ahmed, R. (2019). Prevalence of Metabolic Syndrome and Its Components in Patients of Hypothyroidism in A north Indian Tertiary Care Hospital. GJRA- Global Journal for Research Analysis, 8(5), 6-8.

O'brien, T., Dinneen, S. F., O'brien, P. C., & Palumbo, P. J. (1993). Hyperlipidemia in patients with primary and secondary hypothyroidism. In Mayo Clinic Proceedings, Elsevier, 68(9), 860-866.

Regmi, A., Shah, B., Rai, B. R., & Pandeya, A. (2010). Serum lipid profile in patients with thyroid disorders in central Nepal. Nepal Medical College Journal, 12(4), 253-256.

Saini, V., Yadav, M. A., Arora, S., Singh, R., & Bhattacharjee, J. (2012). Association between different degrees of hypothyroidism and serum lipids. Internet Journal of Medical Update-EJOURNAL, 7(2), 3-8.

Sangeeta, N., Singh, Y. A., Devi, O. P., Singh, R. R., Chubalemla, L., Abhishek, D., Basar, G., Ibrahunlang, R., Devi, N. O., & Singh, M. A. (2016). Lipid Profile in Thyroid Dysfunction Patients. IOSR Journal of Dental and Medical Sciences (IOSR-JDMS), 15(12), 39-43.

Satyanarayana, P., & Kumar, V. (2019). Lipid profile status Assessment in Subjects with Overt and sub clinical hypothyroidism without hypothyroidism. International Journal of Scientific Research, 8(7), 70-72.

Sharma, A., Goyal, A., Sinha, M., & Fiza, B. (2019). Estimation of serum lipid profile in patients with impaired thyroid function. International Journal of Scientific Research 8(8), 47-49.

Shashi, A., & Sharma, N. (2012). Lipid profile abnormalities in hypothyroidism. International Journal of Science and Nature, 3(2), 354-60.

Shekhar, R., Srinivas, C. H., & Das, M. C. (2011). Lipid profile in 'newly diagnosed' and 'on treatment' hypothyroid. Journal of Clinical and Diagnostic Research, 5(5), 998-1000.

Shilpashree, M. K. (2012). Study of serum lipoprotein (a) and lipid profile in hypothyroidism. (Doctoral dissertation, RAJIV Gandhi University of Health Sciences Bangalore, Karnataka),1-111.

Singh, S., & Sarkar, D. P. (2014). Serum lipids, tHcy, hs-CRP, MDA and PON-1 levels in SCH and Overt hypothyroidism: effect of treatment. Journal of Acta Biomed, 85(2), 127-134.

Thompson, G. R., Soutar, A. K., Spengel, F. A., Jadhav, A., Gavigan, S. J., & Myant, N. B. (1981). Defects of receptor-mediated low-density lipoprotein catabolism in homozygous familial hypercholesterolemia and hypothyroidism in vivo. Journal Proceedings of the National Academy of Sciences, 78(4), 2591-2595.

Tzotzas, T., Krassas, G. E., Konstantinidis, T., & Bougoulia, M. (2000). Changes in lipoprotein (a) levels in overt and subclinical hypothyroidism before and during treatment. Journal of Thyroid, 10(9), 803-808.

Vanderpump, M., & Mark, P. J. (2011). The epidemiology of thyroid disease. Journal of British medical bulletin, 99(1), 39-51.

Wanjia, X., Chenggang, W., Aihong, W., Xiaomei, Y., Jiajun, Z., Chunxiao, Y., Jin, X., Yinglong, H., & Ling, G. (2012). A high normal TSH level is associated with an atherogenic lipid profile in euthyroid non-smokers with newly diagnosed asymptomatic coronary heart disease. Lipids in health and disease, 11(44), 1-8.

Wung, S. F., Kulkarni, M. V., Pullinger, C. R., Malloy, M. J., Kane, J. P., & Aouizerat, B. E. (2006). The lipoprotein lipase gene in combined hyperlipidemia: evidence of a protective allele depletion. Journal of Lipids in health and disease, 5(1), 19,1-8.

Yousif, B. M. (2001). Determination of some Trace Elements in Serum of Hyperthyroidism and Hypothyroidism patients. (Doctoral dissertation, University of Khartoum), 1-95.

Zhenjiang, H., Zhaoxin, M., Jingyu, Z., Hong, F., & Jianzhang, H. (2017). The Correlation of Blood Lipid Profile and its Ratio, Cystatin C and Homocysteine of Thyroid Dysfunction. American Journal of Clinical and Experimental Medicine, 5(4), 108-114.

Zhu, X., & Cheng, S. Y. (2010). New insights into regulation of lipid metabolism by thyroid hormone. Journal of Current opinion in endocrinology, diabetes, and obesity, 17(5), 408-413.

Zimmermann, M. B. (2009). Iodine deficiency. Journal of Endocrine Reviews, 30(4), 376-408.