

Hyperhomocysteinemia in Patients with Hypothyroidism

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ABSTRACT

Objective: To determine the hyperhomocysteinemia in patients with hypothyroidism.

Study Design: Cross Sectional Descriptive Study

Place and Duration of Study: This study was conducted at the Liaquat University Hospital Hyderabad from January 2018 to December 2018.

Materials and Methods: The inclusion criteria were the patients of age ≥ 18 year, either gender and aged 18 years and newly diagnosed case of hypothyroidism (TSH >15 mU/l) while the exclusion criteria were the patients with <18 yrs, already on thyroid replacement therapy and vitamin B12 and folic acid, the subjects with subclinical hypothyroidism, the individuals who developed hypothyroidism as a result of thyroidectomy or radioablation, the patients already on phenytoin, phenobarbitone and valproate, niacin and cholestyramine. The relevant and specific investigations were advised and 2 ml venous blood was taken after aseptic measure and sent to laboratory for serum homocysteine level. The frequency and percentages were computed for categorical variables whereas the mean \pm SD was computed for numerical variables.

Results: During one-year study period total fifty patients with hypothyroidism were recruited and studied had mean age \pm SD identified as 47.87 ± 7.52 (yrs) with female gender predominance 34 (68%). Regarding residence, the urban and rural population was identified as 22 (44%) and 28 (56%) while the clinical features observed were weight gain 42 (84%), fatigue 30 (66%), puffiness of face 28 (56%), leg swelling 23 (46%), cold intolerance 18 (36%). the hyperlipidemia was observed in 30 (60%) while the other comorbidities observed were diabetes mellitus 35 (70%), hypertension 28 (56%), obesity 23 (46%), osteoporosis 21 (42%) whereas the hyperhomocysteinemia was observed in 32 (64%) patients respectively.

Conclusion: The patients with hypothyroidism are at risk for hyperhomocysteinemia and dyslipidaemia and are more prone to premature atherosclerosis and increased adverse cardiovascular events.

Key Words: Thyroid, Hypothyroidism, Homocysteine, Lipid, Hyperlipidemia and Dyslipidemia

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INTRODUCTION

The thyroid name was derived from Greek language and the thyroid hormones are important for growth and development of a human being.¹ The thyroid gland weighs 15 to 20 grams while the thyroid gland is composed of two lobes connected by a thin tissue bands called as isthmus.² The hypothyroidism due to iodine deficiency remains the leading etiology for hypothyroidism.³

Thyroid disease is associated with atherosclerotic cardiovascular disease and may be due to thyroid

hormones regulation of fat metabolism and its effects on blood pressure.^{4,5} Thyroid hormones have various effects and influence the function of most organs.⁶ Coronary artery atherosclerosis is common observed in individuals with hypothyroidism while the adequate thyroid hormone replacement may have protective effect on the progression of disease.⁷ The atherogenic profile of fat and the hyper-homocysteinemia in hypothyroid patients suggest greater risk of coronary atherosclerosis in such population.^{8,9} The evidence of association between homocysteine and coronary artery disease was given by Wilcken EL, et al.¹⁰ The study conducted by Shalooob M et al shown 16.88% individuals found to have serum homocysteine level of $>20 \mu\text{mol/L}$.¹¹

Thus, in the light of above facts, this study aimed to explore the association between the homocysteine levels and thyroid disturbance (hypothyroidism) at tertiary care teaching hospital. Hyperhomocysteinemia is the risk factors for atherosclerosis and cardiovascular deaths in hypothyroidism and by timely exploration and diagnosis along with abrupt treatment of thyroid dysfunction, the burden of complications,

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morbidity and mortality associated with hypothyroidism in relation to atherosclerosis can be reduced.

MATERIALS AND METHODS

The cross sectional descriptive study was conducted from January 2018 to December 2018 at Liaquat University Hospital Hyderabad. Total fifty cases were selected from the Medicine and allied ward with clinical presentation suggestive of hypothyroidism. After revealing the need for relevant investigations and necessity for further management, the patients were recruited by having informed consent obtained from patient or attendant before including the participant in the study. The inclusion criteria were the subjects of age ≥ 18 year, either gender and newly diagnosed case of hypothyroidism (TSH $> 15\text{mU/l}$) while the exclusion criteria were the patients with $< 18\text{yrs}$, already on thyroid replacement therapy and vitamin B12 and folic acid, the subjects with subclinical hypothyroidism, the individuals who developed hypothyroidism as a result of thyroidectomy or radioablation, the patients already on phenytoin, phenobarbitone and valproate, niacin and cholestyramine. The demographical profile was inquired while the clinical examination was performed and recorded on pre-designed proforma. The relevant and specific investigations were advised and 2 ml venous blood was taken after aseptic measure and sent to laboratory for serum homocysteine level while the data was analyzed in SPSS 21. The frequency and percentages were computed for categorical variables whereas the mean \pm SD was calculated for numerical variables.

RESULTS

During one-year study period total fifty patients with hypothyroidism were recruited and studied had mean age \pm SD identified as 47.87 ± 7.52 (yrs) with female gender predominance. The demographical and clinical profile of study population is presented in Table I.

Table No.1: The Demographical and Clinical Profile of Study Population

Parameter	Frequency (N=50)	Percentage (%)
AGE (yrs)		
12-19	06	12
20-29	09	18
30-39	16	32
40-49	19	38
GENDER		
Male	16	32
Female	34	68
RESIDENCE		
Urban	22	44
Rural	28	56
HYPERLIPIDEMIA		

Yes	30	60
No	20	40
SYMPTOMS		
Weight gain	42	84
Fatigue	30	66
Puffiness of face	28	56
Leg swelling	23	46
Cold intolerance	18	36
CO-MORBIDS		
Diabetes mellitus	35	70
Hypertension	28	56
Obesity	23	46
Osteoporosis	21	42
HYPERHOMOCYSTEINEMIA		
Yes	32	64
No	18	36

DISCUSSION

The prevalence of hypothyroidism directly proportion to age and more predominant in female population while Turhan S, et al raised the research question of a association between atherosclerosis and hypothyroidism.¹² Thyroid disturbance is associated with atherosclerotic CV disease and has various adverse effects on heart and blood pressure.¹³ Hypothyroidism composed of multiple metabolic risk factors that initiates atherosclerosis and adverse cardiovascular events.¹⁴ The hypothyroidism is associated with co-morbidities as obesity, overweight, hypertension, diabetes and hyperlipidemia.¹⁵ Hypothyroid patients with subclinical picture, drug compliance and lately diagnosis of hypothyroidism associated with metabolic syndrome.¹⁶ Asvold BO, et al in his study found the positive relationship of TSH within serum fat concentration.¹⁷ The atherogenic profile of serum lipids and hyperhomocysteinemia in hypothyroid patients suggests greater risk for ischemic heart diseases, cerebrovascular accidents and young age mortalities.¹⁸ Al-Habori M, et al conducted a study in Kuwait comprised fifty patients with hypothyroidism, the age stratification was between 25 to 64 years with mean \pm SD 39.2 years and entire population was female.¹⁹ Al-Habori M, et al study comprised 50 patients with hypothyroidism and significant rise in serum homocysteine in hypothyroid subjects than in control groups was observed respectively.¹⁹ Thus, the association of lipid disturbance and hyperhomocysteinemia observed in hypothyroid individuals may represent a dynamic atherogenic state responsible for adverse cardiovascular events.

CONCLUSION

The Thyroid dysfunction is common in Pakistani population while the TSH is directly proportional to serum homocysteine levels. The patients with hypothyroidism are at risk for hyperhomocysteinemia

and dyslipidaemia and are more prone to premature atherosclerosis and increased adverse cardiovascular events.

Author's Contribution:

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REFERENCES

- Niazi AK, Kalra S, Irfan A, Islam A. Thyroidology over the ages. *Ind J Endocrinol Metab* 2011;15(Suppl 2):S121-S126.
- Barmpari ME, Kokkorou M, Micheli A, Alexiou I, Spanou E, Noutsou M, et al. Thyroid Dysfunction among Greek Patients with Type 1 and Type 2 Diabetes Mellitus as a Disregarded Comorbidity. *J Diabetes Res* 2017;2017:6505814.
- Kostoglou-Athanassiou I, Ntalles K. Hypothyroidism - new aspects of an old disease. *Hippokratia* 2010;14(2):82-87.
- Ichiki T. Thyroid hormone and atherosclerosis. *Vascul Pharmacol* 2010;52(3-4):151-6.
- Cappola AR, Ladenson PW. Hypothyroidism and atherosclerosis. *J Clin Endocrinol Metab* 2003;88(6):2438-44.
- Saif A, Mousa S, Assem M, Tharwat N, Abdelhamid A. Endothelial dysfunction and the risk of atherosclerosis in overt and subclinical hypothyroidism. *Endocr Connect* 2018;7(10):1075-1080.
- Auer J, Berent R, Weber T, Lassnig E, Eber B. Thyroid function is associated with presence and severity of coronary atherosclerosis. *Clin Cardiol* 2003;26(12):569-573.
- Sengül E, Cetinarslan B, Tarkun I, Cantürk Z, Türemen E. Homocysteine concentrations in subclinical hypothyroidism. *Endocr Res* 2004;30(3):351-9.
- Zhang Y, Wang Q, Li Q, Lu P. Association between Hyperhomocysteinemia and Thyroid Hormones in Euthyroid Diabetic Subjects. *Biomed Res Int* 2015;2015:196379.
- Wilcken DEL, Wang XL, Adachi T. Relationship Between Homocysteine and SuperoxideDismutase Homocystinuria Possible Relevance to Cardiovascular Risk. *Arterioscler Thromb Vasc Biol* 2000;20:1199-1202.
- Shalooob M, Cherian A, Murthy JSN, Muralidharan TR, Manokar P, thanikachalam S. Oral presentations. Prevalence of hyperhomocysteinemia in the south indian population. *J Assoc Physicians Ind* 2006;54:775-82.
- Turhan S, Sezer S, Erden G, Guctekin A, Ucar F, Ginis Z, et al. Plasma homocysteine concentrations and serum lipid profile as atherosclerotic risk factors in subclinical hypothyroidism. *Ann Saudi Med* 2008;28(2):96-101.
- Zhou Y, Chen Y, Cao X, Liu C, Xie Y. Association between plasma homocysteine status and hypothyroidism: a meta-analysis. *Int J Clin Exp Med* 2014;7(11):4544-4553.
- Diekmann MJ, van der Put NM, Blom HJ, Tijssen JG, Wiersinga WM. Determinants of changes in plasma homocysteine in hyperthyroidism and hypothyroidism. *Clin Endocrinol (Oxf)* 2001;54(2):197-204.
- Orzechowska-Pawilojc A, Sworczak K, Lewczuk A, Babinska A. Homocysteine, folate and cobalamin levels in hypothyroid women before and after treatment. *Endocr J* 2007;54(3):471-6.
- Orluwene CG, Mommoh MO. Plasma total homocysteine, high-sensitivity C-reactive protein and thyroid function in metabolic syndrome patients. *Niger Postgrad Med J* 2013;20(4):286-90.
- Asvold BO, Bjoro T, Nilsen TIL, Vatten LJ. Association between Blood Pressure and Serum Thyroid-Stimulating Hormone Concentration within the Reference Range: A Population-Based Study. *J Clin Endocrinol Metabol* 2007;92(3):841-845.
- Lien EA, Nedrebo BG, Varhaug JE, Nygård O, Aakvaag A, Ueland PM. Plasma total homocysteine levels during short-term iatrogenic hypothyroidism. *J Clin Endocrinol Metab* 2000;85(3):1049-53.
- Al-Habori M, Al-Meerri A, Al-Nuzaily MA, Ali F. Homocysteine Level in Relation to Thyroid Function Tests in Hypothyroid Patients. *Asian J Med Pharm Res* 2014;4(2):101-106.