

Study of Various Biochemical Parameters in Patients of Myopathy with Hypothyroidism

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Abstract:

Background: Thyroid dysfunctions are common endocrine disorders. Muscle involvement in hypothyroidism is common with 30-80% of hypothyroid patients presenting with muscular symptoms varying from myalgia to true myopathy. **Aims & objective:** The aim of this study was to find out relationship of various biochemical parameters in patient's of myopathy with hypothyroidism. **Materials and Methods:** The present study was conducted on 100 hypothyroid patients attending the Medical OPD and Radio Immuno Assay (RIA) Laboratory of the Biochemistry Department of JLN Medical College & Hospitals, Ajmer, after taking approval from ethical committee. The results of patients were compared with 50 healthy control subjects of either sex of similar age group. The blood samples were collected from all the attending patients and analyzed for Various Serum Muscle Markers. These values were compared by P value. **Results:**All the muscle markers fraction were comparable to those of studied groups and they were significantly deranged, as compared to those of Group-I. A significant

increased in the levels of CK-NAC, LDH, AST and Myoglobin and non significant elevated level of CK-MB was observed in hypothyroid subjects as compared to the healthy control subjects. **Conclusion :** We found that these muscle markers along with thyroid profile can be used to determine the severity as well as for screening and early diagnosis of hypothyroidism and any associated underlying myopathy.

INTRODUCTION:

Thyroid dysfunction is one of the most common endocrinological disorders. Consequently, abnormalities of these hormones frequently involve many organ systems producing diverse clinical signs and symptoms which are generally nonspecific. Thus confirmation of a provisional diagnosis of thyroid disorder rests largely upon biochemical parameters [25]. The patients with hypothyroidism do have myopathy rather than functional muscle disease. Nonspecific muscle stiffness related to myalgia may be associated with serum muscle enzyme elevations. Serum creatine kinase (CK) was first used as a

diagnostic aid in progressive muscular dystrophy in 1959 by Ebashi et al [4]. It has since become an important clinical marker for muscle damage. The serum CK level in healthy individuals depends on age, race, lean body mass and physical activity [16]. Serum creatine kinase (CK) elevation can be observed in 57%–90% of patients with hypothyroidism [3]. CK MB- one of the iso forms of CK, is a marker for diagnosis of myocardial infarction. It is also increased in various inflammatory conditions of skeletal muscles and muscle damage and along with CK and troponin levels has also been reported to increase above reference values in hypothyroid patients without apparent myocardial damage [8]. Skeletal muscle is affected more profoundly in cases of overt hypothyroidism and less so when subclinical hypothyroidism is present [20]. A majority of patients with hypothyroidism have been shown to have an increased serum CK. Furthermore only a few studies have investigated serum lactate dehydrogenase (LDH) and aspartate transaminase (AST/SGOT) activity in patients with thyroid dysfunction. The present study was carried out to various serum muscle markers (creatine kinase, creatine kinase-MB(CK-MB), LDH, AST & myoglobin) in cases of hypothyroidism and to correlate their levels with tri-iodothyronine (T3), thyroxine (T4) and thyroid stimulating hormone (TSH) levels.

Myoglobin is a cytoplasmic protein in striated cardiac and skeletal musculature that is involved in oxygen transport and storage within the myocytes. Elevated myoglobin values can also occur after skeletal muscle damage in patients with myopathy and in those with marked renal impairment [19].

MATERIAL AND METHODS: The present study was conducted on 100 hypothyroid patients (Group II) attending the Medical OPD and Radio Immuno Assay (RIA) Laboratory of the Biochemistry Department of JLN Medical College & Hospitals, Ajmer. The results of patients were compared with 50 healthy control (Group I) subjects of either sex of similar age group. Blood samples were collected by venipuncture by aseptic technique. The serum separated from the samples were analyzed for following biochemical parameters. Serum levels of T3, T4 and TSH were measured by RIA method. The serum muscle markers were estimated (by the NAC Kinetic UV method for Creatine kinase, by the Immunoinhibition Kinetic UV method for CK-MB, by the Pyruvate kinetic UV method for LDH, by the NADH, Kinetic UV, IFCC Method for by the ELISA method for Myoglobin), after taking approval from ethical committee. SPSS.13/win statistical software was used for analyzing the data. The results were expressed as mean \pm standard deviation (SD). P-value $<$ 0.05 was considered statistically significant.

RESULTS: The present study had been concluded on 150 subjects with age group (25-55 years). These were further divided into 2 groups. Group I comprised of 50 subjects who were

euthyroid (control), Group II comprised of 100 subjects who were hypothyroid patients.

Table no.1: Levels of serum T3, T4 & TSH in study population.

| Variables (Normal Range) | Control (Mean ± SD) | Study Group (Mean ± SD) | p value |
|--------------------------------------|------------------------|----------------------------|-----------|
| Total T3 (0.7-1.2.0 ng/ml) | 1.11 ± 0.35 | 0.43 ± 0.2 | 0.0001 ** |
| Total T4 (5.5-13.5µg/ml) | 7.59 ± 1.58 | 3.6 ± 1.4 | 0.0001 ** |
| TSH (0.17-4.05µIU/ml) | 2.79 ± 1.22 | 32.0 ± 12.1 | 0.0001 ** |

[NS: p > 0.05: Not Significant; * p < 0.05: Significant; ** p < 0.001: Highly Significant.]

Table no. 2: Comparison of serum CK, CKMB, LDH, AST & myoglobin levels between control and study groups.

| Variables (Normal Range) | Control (Mean ± SD) | Study Group (Mean ± SD) | p value |
|------------------------------|------------------------|----------------------------|-----------|
| CK-NAC (24-195 IU/L) | 106.75 ± 34.89 | 230.9 ± 89.0 | 0.0001** |
| CK-MB(0-25IU/L) | 10.27 ± 3.35 | 11.8 ± 5.6 | 0.21NS |
| LDH(230-460 IU/L) | 155.79 ± 29.50 | 243.5 ± 70.90 | 0.0001 ** |
| AST/SGOT(0-37 IU/L) | 20.01 ± 7.61 | 45.3 ± 25.7 | 0.0001** |
| Myoglobin (0-77ng/ml) | 16.8±5.5 | 39.5±22.5 | 0.0001** |

[NS: p > 0.05: Not Significant; * p < 0.05: Significant; ** p < 0.001: Highly Significant.]

Table:1 illustrates the Mean ± SD levels of T3 and T4 were lower in the hypothyroid subjects, even with elevated serum TSH levels. Serum thyroid profile was observed statistically highly significant (p<0.0001) in hypothyroid subjects when compared with euthyroid subjects. **Table:2** shows a significant increased in the levels of CK-NAC, LDH, AST and Myoglobin and non significant elevated level of CK-MB

was observed in hypothyroid subjects as compared to the healthy control subjects.

DISCUSSION: The increase in CK in hypothyroidism can be explained by various mechanisms. The hypometabolic state of hypothyroidism can cause reduction in glycolysis and oxidative phosphorylations and thus reducing adenosine triphosphate (ATP) concentration beyond a critical limit. The alteration in sarcolemmal

membranes can cause increased cell permeability and the leakage of CK from cells. [15,22,23]. Another possibility is reduced turnover of CK because of hypothyroidism, allowing serum activity to rise generating a marked release of CK through the altered sarcolemmal membranes [15, 18]. Some patients with primary hypothyroidism may have a marked myopathy [14] with associated histological changes in muscle cells [21]. It is widely suggested that increase results from leakage of the enzyme from muscle cells [13] related to subnormal body temperature accompanying primary hypothyroidism [18]. The increase may also reflect a decrease in enzyme clearance [10]. Hypothyroid patients have increase activity of serum creatine kinase that is mostly due to increase CK-MM as CK isoenzyme analysis in six cases of primary hypothyroidism showed only the MM isoenzyme to be present in four patients, and MM with a trace of MB in the other two [15]. This finding also confirms previous studies that indicated skeletal muscle to be the major source of the increase plasma CK activity [1,15] Hypothyroid patients have increased concentration of creatine kinase that is mostly due to increased CK-MM. However, CK-MB has also been reported to increase above reference values in hypothyroid patients without apparent myocardial damage [7,26]. The study also found increase in LDH and AST/SGOT activity in patients with overt

hypothyroidism. Fleisher GA et al also reported 37% of hypothyroid patients to have elevated LDH levels [5] . In another study elevation of LDH activity was found in 33% of patients with overt hypothyroidism and in 74% of patients with subclinical hypothyroidism² and in a latter study 27 of 45 hypothyroid patients had elevated total LDH levels [28]. The levels of AST/SGOT were reported to be elevated in 60% of patients with hypothyroidism by Griffith PD [6]. .Involvement of skeletal muscle is among the most prevalent clinical consequences of hypothyroidism. Histologically the muscle fibres show enlargement, focal myofibrillar degeneration, increase in central nuclei, glycogen accumulation and mitochondrial aggregations and type II fibre atrophy [11]. Slowed muscle contraction and relaxation, known as hypothyroid myopathy may be caused by a shift in the distribution of muscle fibre types from fast-twitch fibres to slow-twitch fibres. A reduction in muscle mitochondrial oxidative capacity and beta adrenergic receptors, as well as the induction of an insulin-resistant state, may result in these changes. Evidence from a study by Sinclair and colleagues suggests that a decrease in muscle carnitine in patients with either hypothyroidism or hyperthyroidism may contribute to thyroid myopathy [27]. In comparison with other studies, Mortino et al.[17] observed significantly higher serum myoglobin levels in long-term and short-term hypothyroid patients

(examined 20 days after withdrawal of thyroid replacement therapy) than normal controls, with a significant inverse correlation between thyroid hormones and myoglobin levels in long-term, but not short-term, hypothyroids. Normalisation of myoglobin levels following thyroxine replacement was achieved earlier than serum TSH, hence, the duration and severity of hypothyroidism are important factors in the rise of myoglobin. Roti et al.[24] also reported high and low serum concentrations of myoglobin, creatine kinase and lactate dehydrogenase in hypothyroid and hyperthyroid patients respectively. It seems that patients with hypothyroidism may occasionally be prone to muscle damage leading to myopathy or even rhabdomyolysis which can be attributed to undiagnosed hypothyroidism. The spectrum of presentation, as a consequence of muscle involvement, may be in the form of asymptomatic elevation of muscle markers, myopathy, rhabdomyolysis or even acute renal failure. Muscle functions usually completely recover with thyroxine therapy [2,9,12].

CONCLUSION: We found that these muscle markers along with thyroid profile can be used to determine the severity as well as for screening and early diagnosis of hypothyroidism and any associated underlying myopathy.

REFERENCES:

1. Archana Prakash, A K Lal, K S Negi. Serum creatine kinase activity

- in thyroid disorders. JK Science; 9(1): 25 -26, Jan mar 2007.
2. Birewar S, Oppenheimer M, Zawada ET Jr. Hypothyroid acute renal failure. S D J Med 2004; 57:109-10.
3. Duyff RF, Van den Bosch J, Laman DM, van Loon BJ, Linssen WH. Neuromuscular findings in thyroid dysfunction: a prospective clinical and electrodiagnostic study. J Neurol Neurosurg Psychiatry 2000;68(6):750-55.
4. Ebashi S, Toyokura T, Momoi H, Sugita H. High Creatine Phosphokinase activity of sera of progressive muscular dystrophy patients. Bioch J Tokyo 1959;46:103.
5. Fleisher GA, McConahey WM, Pankow M. Serum creatine kinase, lactic dehydrogenase and glutamicoxaloacetic transaminase in thyroid diseases and pregnancy. Mayo Clin Proc.1965;40:300-11.
6. Griffith P.D. Serum enzymes in diseases of the thyroid gland. J.clin.Path. 1965;18:660-63.
7. Gunduj H, Arinc H, Yolcu M, Akdemir R, Kanat M, Uyan C. A case of hypothyroidism mimicking acute coronary syndrome. Minerva Endocrinol 2006 June; 31(2): 173-8.
8. Gunduz H, Arinc H, Yolcu M, Akdemir R, Kanat M, Uyan C. A case of hypothyroidism mimicking acute coronary syndrome. Int J Cardiovasc Imaging 2006;22:141-45.
9. Kar PM, Hirani A, Allen MJ. Acute renal failure in a hypothyroid patient with rhabdomyolysis. Clin Nephrol 2003; 60:428-9.
10. Karisberg RP, Roberts B. Effect of altered thyroid function on plasma creatine kinase clearance in dog. Am J Physiol; 235:E614-8, 1978.
11. Khaleeli AA, Gohil K, McPhail G, Round JM, Edwards RHT. Muscle morphology and metabolism in

- hypothyroid myopathy: effects of treatment. *J Clin Pathol.*1983;36:519-26.
12. Kisakol G, Tunc R, Kaya A. Rhabdomyolysis in a patient with hypothyroidism. *Endocr J* 2003; 50:221-3.
 13. Klein I, Mantell P, Parker M, Levey GS. Resolution of abnormal muscle enzyme studies in hypothyroidism. *AM J Med Sci*; 279:159-62, 1980.
 14. Mace BE, Mallya RK, Staifurth JS. Severe myxedema presenting with chondrocalcinosis and polymyositis. *JR Soc Med*; 73:887-8, 1980.
 15. McGroder DA, Fraser YP, Gorden L, TV Crawford, JM Rawlins. Serum creatine kinase and lactate dehydrogenase activities in patients with thyroid disorders. *Nigerian Jr of clinical Practice*; 14(4): 454 - 459, oct dec 2011.
 16. Meltezer H.Y. Factors affecting creatine phosphokinase levels in the general population. The role of race, activity and age. *Clin Chem Acta* 1971;33:165-72.
 17. Mortino E, Sardano G, Vaudagna G, Bambini G, Breccia M, Motz E, et al. Serum myoglobin in primary hypothyroidism and effect of L-thyroxine therapy. *J Nucl Med* 1982; 23:1088-92.
 18. O'Malley BP, Davies TJ, Rosenthal FD. Effects of rest, exercise and warming on serum creatine kinase levels in primary hypothyroidism. *Clin Sci*; 60:595-7, 1981.
 19. Ohman EM, Casey C, Bengston JR, Pryor D, Tormey W, Horgan JH. Early detection of acute myocardial infarction: additional diagnostic information from serum concentrations of myoglobin in patients without ST elevation. *Br Heart J* 1990; 63:335-8.
 20. Panag KMDS, Gitanjali, Goyal S. Evaluation of Creatine Kinase as a Diagnostic Tool for Thyroid Function. *Indian Journal of Clinical Practice* 2012;23(4):221-23.
 21. Rainsay I. Thyroid disease and muscle dysfunction. London: Heinemann Medical Books Ltd; 1974.
 22. Robinson JM, Wilkinson JH, Jhonson KP. Factors affecting the release of hemoglobin and enzymes from human erythrocytes. *Ann Clin Biochem*; 12:58-65, 1974.
 23. Robinson JM, Wilkinson JH. Effect of energy-rich compounds on reasease of intracellular enzymes from human leucocytes and rat lymphocytes. *Clin Chem*; 20:1331-6, 1974.
 24. Roti E, Bandini P, Robuschi G, Emanuele R, Ciarlini E, Buzzonetti P, et al. Serum concentrations of myoglobin, creatine kinase, lactate dehydrogenase and cardiac isoenzymes in euthyroid, hypothyroid and hyperthyroid subjects. *Ric Clin Lab* 1980; 10:609-17.
 25. Saha M, Sarkar P, Chattopadhyay R, Mukhopadhyaya M, Bhowmick K. Role of creatine kinase and its coenzymes as surrogate markers of thyroid function. *IJMB* 2009;13(2):10-4.
 26. Satar S, Seydoglu G, Avci A, Sebe A, Karcioglu O, Topal M. Prognostic value of thyroid hormone levels in acute myocardial infarction. *Int J Cardiovasc Imaging* 2006 ; 22(2): 141-5.
 27. Sinclair C, Gilchrist JM, Hennessey JV. Muscle carnitine in hypo and hyperthyroidism. *Muscle Nerve* 2005;32(3):357-59.
 28. Strasberg GD. Hypothyroidism and Isozyme Elevations. *Arch Intern Med.*1984;144:1313.