Serum Myoglobin in Patients with Thyroid Dysfunction

*Waad-Allah S Mula-Abed, Sawsan S Al-Sinani, Huda S Al-Hashmi

ABSTRACT

Objectives: To assess the pattern of change in serum myoglobin concentration in subjects with thyroid dysfunction.

Methods: Serum samples were selected from 150 subjects with suspected thyroid disorder who were referred to the Royal Hospital, Muscat, Oman. The subjects were 35 males and 115 females, aged 14-56 years with mean ± SD of 34.3 ± 12.7 years. They were classified on the basis of thyroid stimulating hormone (TSH) and free thyroxine (FT4) into 3 groups, each consisting of 50 subjects: hypothyroid, hyperthyroid, and euthyroid subjects.

Results: The mean serum myoglobin concentration was higher in hypothyroid patients compared to hyperthyroid and euthyroid subjects (mean ± SD was 38.5 ± 23.1 µg/L in hypothyroid; 18.1 ± 7.09µg/L in hyperthyroid; 17.4 ± 5.7µg/L in euthyroid). There was a significant difference in myoglobin concentration between hypothyroid and euthyroid groups (F = 36.1, p < 0.001), however, there was no significant difference between the hyperthyroid and euthyroid groups. When the mean ± 2SD for myoglobin in euthyroid subjects was calculated, the reference range was 6-29 µg/L. Of the hypothyroid subjects, 29 (58%) had high myoglobin and 21 (42%) had normal myoglobin level. No significant correlation was noticed between TSH or FT4 and myoglobin in all studied subjects. Conclusion: Raised serum myoglobin may be observed in patients with hypothyroidism. Hence hypothyroidism should be considered in the differential diagnosis of patients with raised serum myoglobin concentration.

Key words: Myoglobin; Hypothyroidism.

Advances in Knowledge

- Elevated myoglobin values can occur following muscle involvement or damage in patients with myopathy or transiently following cardiac ischaemia.

Department of Chemical Pathology, Royal Hospital, Muscat, Sultanate of Oman

*To whom correspondence should be addressed. Email: drsharef@omantel.net.om
Myoglobin is a cytoplasmic protein in striated cardiac and skeletal muscle structure that is involved in oxygen transport and storage within the myocytes. Besides troponin, myoglobin determination in serum may play a contributing step in the diagnosis of myocardial ischaemia particularly acute myocardial infarction.\(^1,\)\(^2\) Elevated myoglobin values can also occur after skeletal muscle damage in patients with myopathy and in those with marked renal impairment.\(^3\)

Disorders of thyroid function are common and are now considered in the differential diagnosis of patients with a wide variety of symptoms. The prevalence of hypothyroidism was 3.7% and that of hyperthyroidism was 0.5% in the United States general population in a 1999-2002 survey.\(^4\) The prevalence of thyroid dysfunction is even higher in the elderly,\(^5\) many having subclinical thyroid dysfunction with controversial recommendations for treatment thresholds balanced on the risk to target organs particularly the heart and bone.\(^6\) Hence, screening for thyroid problems is now commonly followed in clinical practice.\(^7\) However, although biochemical screening for thyroid disorders is usually followed, particularly in the elderly, the clinical diagnosis of hypothyroidism should also be considered in patients with unexplained persistent elevations of serum muscle enzymes. A significant increase in these enzymes may occur in basal conditions and is gradually normalised by substitution therapy.\(^8,\)\(^9\)

The objective of this study was to assess the pattern of change in serum myoglobin concentration in patients with thyroid disorders, both hypothyroidism and hyperthyroidism, and to compare them with euthyroid subjects.

**Methods**

In this study, 150 tests from routine sampling were selected on the suspicion of thyroid disorders and underwent a thyroid function test (TFT), which included measurement of free thyroxine (FT4) and thyroid stimulating hormone (TSH). The study was a naturalistic observation, an integral part of routine clinical procedure. The blood samples for these subjects were selected from those referred to the Department of Chemical Pathology, Royal Hospital, Muscat, Oman, for TFT during a period of 6 months (1 Jan to 30 June 2007). The criteria for selection included patients with no other diseases or abnormal clinical or laboratory tests other than thyroid related problems. Of these subjects, 32 were referred from the Outpatient Department at the Royal Hospital and 118 were from Primary Health Centres within the Muscat Region. The subjects were 35 males and 115 females, aged 14-56 years with mean ± SD of 34.3 ± 12.7 years. They included 50 patients with hypothyroidism (12 males, 38 females, aged 20-56 years, 38.0 ± 13.9 years), 50 patients with hyperthyroidism (15 males, 35 females, aged 14-56 years with 34.0 ± 10.6 years), and 50 subjects with euthyroid state (8 males, 42 females,
Aged 15-54 years, 32 ± 12.4 year). Hypothyroidism was defined as raised TSH (>10.0 mU/L) with low (or low-normal) FT4, while hyperthyroidism was defined as suppressed TSH (<0.010) with raised FT4. 10

All serum samples were assayed for FT4 and TSH, and following the definition of the subject as hypothyroid, hyperthyroid or euthyroid, serum was then assayed also for myoglobin. Serum FT4 and TSH were measured by a chemiluminescent microparticle immunoassay (CMIA) on the Architect 2000 System (Abbott, USA). 11, 12 The TSH assay is an ultrasensitive third generation assay with analytical sensitivity of 0.003 mU/L. Serum myoglobin was measured by an electrochemiluminescent immunoassay (ECLIA) on the Roche Cobas e 411 immunoassay analyser (Roche/Hitachi, Germany). 13

The statistical methods included descriptive statistical analyses that comprise the mean, standard deviation (SD), and range (minimum-maximum). One-sample Kolmogorov-Smirnov analysis was used for identifying the pattern of distribution of myoglobin in each group while one way ANOVA (one way analysis of variance) was used to compare the differences in the means of myoglobin concentrations between the groups. A correlation study was also done to compare between myoglobin and TSH or FT4 concentrations. 14 Statistical significance was assigned for \( p < 0.05 \).

**RESULTS**

The results of data analysed are presented according to the grouping of subjects based on TFT as in Table 1. The use of one-sample Kolmogorov-Smirnov analysis revealed a normal distribution in serum myoglobin concentration in each of the three groups. One way ANOVA revealed a significant difference (F = 36.1, \( p < 0.001 \)) in means of myoglobin concentrations between the hypothyroid (38.5 ± 23.1 µg/L) and euthyroid (17.4 ± 5.7 µg/L) groups. However, there was no significant difference in mean serum myoglobin concentration between the hyperthyroid and euthyroid groups.

When the mean ± 2SD for myoglobin concentration in the euthyroid subjects was calculated (Figure 1), the reference range was 6-29 µg/L. Of the hypothyroid subjects, 29 (58%) had a high myoglobin and 21 (42%) had a normal myoglobin level. No significant correlation was noticed between TSH or FT4 and myoglobin in all studied subjects (\( p > 0.05 \)). The distribution of serum myoglobin in the studied subjects is shown in Figure 1.

**DISCUSSION**

Biochemical screening using different organ profiles, including TFT, is frequently performed for patients consulting clinics or hospitals as part of health care provision. Subclinical or overt hypothyroidism or hyperthyroidism are commonly diagnosed in clinical practice. 4,5,7

In this study, hypothyroid patients showed signifi-
cantly higher mean myoglobin levels in comparison with hyperthyroid or euthyroid subjects. Serum myoglobin levels were higher than the reference range in the euthyroid group in 58% of the hypothyroid patients. This may be explained on the basis that, depending on the degree of hormone deficiency, skeletal muscle involvement may occur in hypothyroidism. Creatine kinase and myoglobin have been proved to be useful indicators of myopathy including that due to hypothyroidism.\textsuperscript{15, 16} They are sensitive for the early detection of muscle involvement due to the metabolic disorder and are closely correlated with the metabolic states of patients.\textsuperscript{16} Another possible mechanism for raised myoglobin in patients with hypothyroidism may be explained by an underlying autoimmune process whereby muscle protein antibodies, especially to myoglobin, myosin and troposin, are frequently present in patients with autoimmune thyroid disease leading to muscle damage.\textsuperscript{17}

In comparison with other studies, Mortino et al.\textsuperscript{18} 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.\textsuperscript{19} also reported high and low serum concentrations of myoglobin, creatine kinase and lactate dehydrogenase in hypothyroid and hyperthyroid patients respectively. They confirmed that the muscle (not cardiac) isoenzymes are the source of increased enzyme activity, a finding that was also confirmed by Giampietro et al.\textsuperscript{16} In our study, as in other reports,\textsuperscript{16, 20} despite the high serum myoglobin concentrations observed in hypothyroidism, no significant correlation was noted between TSH and the muscle markers, creatine kinase or myoglobin. Also, in our study, the hyperthyroid patients clearly exhibited myoglobin levels very approximate (with no significant difference) to those of euthyroid subjects. However, this finding was not in accord with that of Wan Nazainmoon et al.\textsuperscript{21} who found that in both overt and subclinical hyperthyroid patients, serum creatine kinase levels were significantly lower than euthyroid or hypothyroid patients.

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.\textsuperscript{22, 23, 24} Studies, such as those reported by Sekine et al.\textsuperscript{25} suggest that rhabdomyolysis could also occur in patients with hypothyroidism, especially those with poor drug compliance, in combination with other aggravating factors such as exercise. Recently, Kursat et al.\textsuperscript{26} and Kiernan et al.\textsuperscript{27} reported an important link between statin induced rhabdomyolysis and hypothyroidism, both overt and occult forms. Such a link or aggravating factor is of particular concern due to the large number of patients taking statin drugs nowadays worldwide. Hence, statin, when prescribed as a hypolipidaemic drug for patients with dyslipidaemia and an associated or underlying hypothyroidism, may raise their risk for muscle involvement, which is a recognised side effect of statin,\textsuperscript{26, 29} and also may rarely raise their requirement for thyroxine therapy.\textsuperscript{27}

**CONCLUSION**

Raised serum myoglobin may be observed in patients with hypothyroidism. Hence, hypothyroidism should be considered in the differential diagnosis of patients with raised serum myoglobin concentration, even if there is another disease, mechanism or therapy explaining its elevation.

**ACKNOWLEDGEMENTS**

The authors gratefully acknowledge the support of the Royal Hospital, Muscat, for their research.

**CONFLICT OF INTEREST:** None

**REFERENCES**


