INTRODUCTION

Lactate dehydrogenase catalyses the interconversion of pyruvate and lactate with concomitant interconversion of NADH and NAD⁺. It has been noted that various conditions can raise the LDH levels including hypothyroidism which is a highly prevalent disorder. As thyroid hormones are essential for normal organ growth, development function and regulate the basal metabolic rate of all cells, its alteration can affect the entire metabolism and can alter the activity of serum enzymes. There is negotiation regarding the increased levels of LDH in thyroid disorders with some studies stating that LDH can perturb the activity of serum enzymes. The aim of this study was to determine the activity of serum Lactate dehydrogenase (LDH) in thyroid disorders and to evaluate the relationship between LDH and T₃, T₄ and TSH levels.

METHODS

The study comprised of patients who reported for thyroid profile investigations in department of biochemistry, Govt Medical College Amritsar, India. An informed consent was taken from every individual. On the basis of the levels of TSH, according to Indian Thyroid society, 359 individuals under study were divided into four groups as follows:

- Group 1 (n=70): Normal TSH (0.44 – 3.46 µIU/ml)
- Group 2 (n=29): Clinical hyperthyroidism (TSH < 0.1 µIU/ml)
- Group 3 (n=171): Subclinical hypothyroidism (TSH range 3.46 – 10 µIU/ml)
- Group 4 (n=89): Clinical Hypothyroidism (TSH > 10 µIU/ml)

Fasting blood samples collected were allowed to clot and serum was separated for thyroid profile and LDH investigations. In vitro quantitative determination of hormones – T3 (Ingbar et al., 1975), T4 (Atwood, 1978) and TSH (Bristow et al., 1982) was carried out by using direct solid phase enzyme immunoassay based ERBA thyrokit, on ERBA Mannheim LISA scan. LDH was measured with Erba transasia
kits by kinetic method as described by Henry et al. (1960) (Henry, 1960) on Erba XL 300 fully autoanalyser.

**Statistical Analysis**

Collected data was analysed using computer software SPSS (version 16.0). Pearson’s coefficient of correlation was calculated to study the significance of correlation between different parameters. Level of significance used was $p<0.05$.

**RESULTS**

The analysis of data showed the very high prevalence of subclinical stage of hypothyroidism in the population under study. The levels of thyroid hormones showed a significant change in hypothyroid state as compared to normal individuals. This change in the levels of T4 was even significant when compared with hyperthyroid and subclinical hypothyroid individuals. The TSH levels showed a highly significant change (at $p<0.001$) in all the disordered thyroid groups as compared to the normal individuals. Analysis of the LDH levels revealed that there was almost no change in the activity of this enzyme in hyperthyroid state in comparison with the normal state. However the LDH activity increased from (336.3 ± 22.9 IU/l) in normal individuals to (439.2 ± 33.3 IU/l) and (510.0 ± 58.9) in subclinical and clinical hypothyroid individuals with significant change at $p<0.01$ (Table 1).

![Table 1. Levels of T3, T4, TSH & LDH in the study groups](image)

<table>
<thead>
<tr>
<th>Group</th>
<th>T3 (ng/ml) Mean±S.D</th>
<th>T4 (µg/dl) Mean±S.D</th>
<th>TSH (µIU/ml) Mean±S.D</th>
<th>LDH (IU/L) Mean±S.D</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group 1 Normal (n=70)</td>
<td>1.22±0.28</td>
<td>7.90±2.60</td>
<td>2.30±0.7</td>
<td>336.3±22.9</td>
</tr>
<tr>
<td>Group 2 Hyperthyroidism (n=29)</td>
<td>1.11±0.6</td>
<td>7.95±5.04</td>
<td>0.17±0.1**</td>
<td>385.3±41.9</td>
</tr>
<tr>
<td>Group 3 Subclinical Hypothyroidism (n=171)</td>
<td>1.22±0.6</td>
<td>7.81±3.13</td>
<td>6.03±1.8*** ‡‡‡‡</td>
<td>439.16±33.3**</td>
</tr>
<tr>
<td>Group 4 Hypothyroidism (n=89)</td>
<td>1.04±0.73§§§</td>
<td>5.22±3.11****††††††</td>
<td>18.6±3.6***†††††† ‡‡‡‡</td>
<td>510±58.9**</td>
</tr>
</tbody>
</table>

* $p<0.05$ w.r.t Group1  ** $p<0.01$ w.r.t Group1  *** $p<0.001$ w.r.t Group1; † $p<0.05$ w.r.t Group2  ‡‡ $p<0.01$ w.r.t Group2  ‡‡‡ $p<0.001$ w.r.t Group2
§ $p<0.05$ w.r.t Group3 §§ $p<0.05$ w.r.t Group3 §§§ $p<0.05$ w.r.t Group3

No correlation was found between the thyroid hormones and TSH with the activity of LDH enzyme in the hyperthyroid individuals. The T4 hormone showed a non significant negative correlation with the LDH activity, in subclinical hypothyroid and clinical hypothyroid individuals (Table 2).

![Table 2. Correlation Coefficient of the study groups](image)

<table>
<thead>
<tr>
<th>Group</th>
<th>T3</th>
<th>T4</th>
<th>TSH</th>
<th>LDH</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal vs Hyper</td>
<td>p=0.55</td>
<td>p=0.98</td>
<td>p=3.16x10^-5</td>
<td>p=0.5</td>
</tr>
<tr>
<td>Normal vs Sub clinical Hypothyroidism</td>
<td>p=0.90</td>
<td>p=0.75</td>
<td>p=2.22x10^-5</td>
<td>p=0.006</td>
</tr>
<tr>
<td>Normal vs Hypothyroidism</td>
<td>p=0.93</td>
<td>p=2.5x10^-8</td>
<td>p=2.5x10^-25</td>
<td>p=0.012</td>
</tr>
<tr>
<td>Hyper Thyroidism vs Subclinical Hypothyroidism</td>
<td>p=0.39</td>
<td>p=0.88</td>
<td>p=1.06x10^-9</td>
<td>p=0.51</td>
</tr>
<tr>
<td>Hyper Thyroidism vs Hypothyroidism</td>
<td>p=0.66</td>
<td>p=0.009</td>
<td>p=2.6x10^-28</td>
<td>p=0.21</td>
</tr>
<tr>
<td>Hypo Thyroidism vs Subclinical Hypothyroidism</td>
<td>p=0.05</td>
<td>p=2.13x10^-4</td>
<td>p=2.02x10^-49</td>
<td>p=0.29</td>
</tr>
</tbody>
</table>

DISCUSSION

Work done so far relates to changes in serum enzyme levels (including LDH) with changes in thyroid hormone levels showing varying degree of correlations; either positive (Pandey, 2013) or negative (McGrowder, 2011) and majorly in overt hypothyroid patients. Previous studies indicate that LDH can be used as parameter for screening thyroid disorders (mainly overt hypothyroidism). As the studies done so far were small group studies to analyse LDH as a reliable tool for diagnosis and prognosis of the disease; the present study was conducted on 359 individuals to assess serum LDH activity in thyroid disorder including the subclinical stage which was not done so far. An effort was made to find the correlation (if any) that exists between the LDH enzyme and thyroid hormones. The study showed that the activity of LDH increased significantly in individuals having subclinical and clinical stage of hypothyroidism whereas on the contrary clinical hyperthyroid stage showed almost no change in LDH activity; which is in confirmation with previous studies that indicated increased LDH activity in overt hypothyroidism (Pandey, 2013). Liver, muscle and kidney metabolizes thyroid hormones and regulates their systemic endocrine effects; which suggests thyroid dysfunction may disturb liver, muscle, other organ function and vice versa (Biondi, 2005). Also the elevated LDH levels could reflect increased release and/or decreased clearance from the liver (Klein, 1984). There seems to be the involvement of skeletal muscles, which slowed histological changes as a clinical consequences of hypothyroidism (Khaleeli, 1983). These changes may result from reduction in muscle mitochondrial oxidative capacity and β-adrenergic receptors, as well as the induction of an insulin resistant state. It has been observed in our previous study that hypothyroidism is associated with insulin resistance (Kaur, 2014). Therefore we can say that the increased levels of LDH may be increased with the glycemic state of the individual as the rate of glucose disposal is positively correlated with plasma lactate concentration (Yki-Jarvinen, 1990). Consequently, plasma lactate concentration increases during insulin stimulated conditions (Avagaro, 1996 and Qvisth, 2007). In some studies it is indicated that muscles also release increased lactate during hyperinsulimemic conditions but the exact mechanism is unclear (Holmäng, 1998; Natali, 1990). LDH activity in this study correlated with the degree of hypothyroidism; but with no significant correlation with thyroid hormones. Therefore significant elevation of serum LDH activity indicate no direct relation of LDH with thyroid hormones in both clinical and subclinical stages of hypothyroidism with no involvement of LDH in hyperthyroid state.
Conclusion
The activity of LDH raised in both subclinical and clinical stages of hypothyroidism, however no significant correlation was found between thyroid hormones and LDH activity. Moreover hyperthyroidism showed no change in LDH activity. Therefore as discussed above LDH may not be used as a direct parameter for assessing thyroid disorders.

REFERENCES

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