Can Hyperlactatemia be an Early Indicator of Adverse Outcomes Post Coronary Artery Bypass Surgery in Subjects with Thyroid Disorder?

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Abstract-
Objective: Hyperlactatemia is increase in the blood lactate levels. It is often observed after critical illness, which involves cardiac surgery as well. Several studies have linked hyperlactatemia with serious medical complications, major morbidity and also death. This study investigated the prognostic potential of hyperlactatemia specifically in subjects having thyroid disorder, who are undergoing coronary artery bypass surgery.

Material and methods: After applying the selection criteria, 560 subjects were finalized for the study. They were divided into 3 groups (hyperthyroid, hypothyroid and euthyroid). Their pre-, intra- and post-operative parameters were collected. Prevalence of hyperlactatemia and its association with these parameters were statistically analysed.

Results: Euthyroid group observed 16.5 % lesser cases of hyperlactatemia. Subjects in thyroid groups (hyper/hypo thyroid) with hyperlactatemia had an average increase of 2 days in ICU stay and total hospitalization, an average increase of 1 day for ventilator support and use of catheter.

Conclusion: Hyperlactatemia can be an early alarm for reporting adverse post-surgery outcomes in subjects undergoing CABG with deranged thyroid status

Keywords- Hyperlactatemia, Cardiac Surgery, Thyroid, Coronary Artery Bypass Graft

1. INTRODUCTION

Globally thyroid disorders are the second most prevalent endocrine diseases, including India (1). The relationship between thyroid status and the cardiovascular system is not unidirectional (2). Cardiovascular effects are the most prominent features of thyroid dysfunction (3). Thyroid diseases are quite prevalent among the people suffering from cardiac diseases (4). Studies indicate that acute and chronic cardiovascular diseases may alter the metabolism of the thyroid hormone (2).Thyroid hormone, in addition to metabolic and thermoregulatory functions, regulates cardiac performance. It has long been recognized that some of the most characteristic and common signs and symptoms of the thyroid disease are those that result from the effects of thyroid hormone on the heart and cardiovascular system (5). Opposite functional thyroid conditions (hypo and hyper) provoke inverse cardiac function changes that, no matter what they are, lead to cardiovascular disease with consequent increased risk of heart failure events (3).

Cardiac surgery may lead to imbalance in oxygen supply and demand leading to tissue hypoxia and finally organ failure (6,7), this will result in increased lactate levels. Higher lactate levels after cardiac surgery are predictors of major complications including early mortality (8). Studies suggest significant elevation in lactate levels in patients with Hypothyroidism (9). In cardiac surgery, increased lactate level both during operation and after transferring the patient to the Intensive care unit (ICU) is associated with poor prognosis (10, 11,12). Studies have shown that absolute lactate value and mean lactate increment were significantly higher in thyroid patients than in controls during exercise (13).

In this study try to provide evidence that hyperlactatemia could be a predictor of adverse outcomes in thyroid patients undergoing CABG.

2. METHODOLOGY

2.1 Study approval- The protocol for this study was approved by the institutional ethical committee (MICR-775/2017). As the consent form used for the surgery clearly stated that the data will be used for the study purpose therefore, need for a separate consent form was waived off.

2.2 Study participants- out of 560 subjects, who underwent CABG and also met the inclusion criteria, 36% had hypothyroid, 5% had hyperthyroid subjects and 330 were euthyroid subjects. As per institutional practice, thyroid test was mandatory so no additional cost was added. Subjects were categorised after the confirmation from an endocrinologist. No interventions were involved in the study.

2.3 Biochemical measurements- ABG was done and recorded in pre-operative period (<2 hours before the surgery) and in post-operative period (at 0 hours when patient reaches ICU) and thereafter at 12, 24 and 48 hours.

2.4 Procedure- Blood sample for atrial blood gas (ABG) were taken from arterial line. ABG was done using a standard 3 ml syringe with 25 –gauge needle. The sealed syringe was immediately taken to RADIOMETERN ABL 800 BASIC (A blood gas analyser machine), which is installed in the ICU. Participant’s demographic details, details of comorbidity, pre-operative, intra-operative and post-operative vitals were recorded. High lactate levels were defined as blood lactate level ≥ 2.5 mmol/l. Lactic
acidosis was defined as blood lactate level ≥ 5.0 mmol/l along with pH< 7.5 (13) which was measured preoperative and post –
operative period.

2.5 Statistical analysis- the statistical analysis included profiling of subjects on different demographic, clinical and laboratory
parameter. For each of these categories quantitative data were recorded in terms of percentages, mean and standard deviations. Means and standard deviations of all the recorded parameters, delta values (postoperative –pre operative value) were calculated. Delta values were compared amongst groups. Peak value (highest value among the observations) was recorded. On the other hand, qualitative/ categorical data were presented as absolute numbers and proportions. Z test was used to compare means of the outcomes. Cross tables were generated and chi-square tests were used to test associations.

3. RESULTS
Derivation of the study, number of patients finally selected for the study after applying the selection criteria is depicted by a flow
chart (Fig 1). On the basis of thyroid hormone status and after confirmation from practising endocrinologist, the selected
participants were divided into three groups, Hypothyroid (Hypo) group, Hyperthyroid (Hyper) group and Euthyroid (Euthy) group. Mean values of thyroid hormones, Thyroid stimulating hormone (TSH), Triiodothyronine (T3) and Thyroxine (T4) in the three groups are summarized in (Table 1).

<table>
<thead>
<tr>
<th>Thyroid hormone</th>
<th>Hypothyroid (202)</th>
<th>Hyperthyroid (28)</th>
<th>Euthyroid (330)</th>
</tr>
</thead>
<tbody>
<tr>
<td>TSH</td>
<td>9.5 ± 1.0</td>
<td>0.24 ± 0.16</td>
<td>2.17 ± 0.9</td>
</tr>
<tr>
<td>FT3</td>
<td>2.87 ± 0.6</td>
<td>3.35 ± 1.38</td>
<td>2.96 ± 0.6</td>
</tr>
<tr>
<td>FT4</td>
<td>1.21 ± 0.4</td>
<td>1.52 ± 0.06</td>
<td>1.34 ± 0.5</td>
</tr>
</tbody>
</table>

Table1. Mean values of TSH, T3 and T4 in Hypothyroid, Hyperthyroid and Euthyroid group.
A total of 1500 participants were initially enrolled. 940 participants were excluded on the basis of exclusion criteria and finally 560 were selected for further analysis. Demographic details and common comorbidities observed in subjects among all three groups are listed in Table 2. Demographic details include information about age, sex and body mass index (BMI) of the subject. Common comorbidities include diabetes mellitus (DM), hypertension (HT), chronic obstructive pulmonary disease (COPD) and chronic kidney disease (CKD).

![Table 2](https://example.com/table2.png)

Table 2. Demographic details and comorbidities observed of all subjects in three groups.

Most of the comorbidities (DM, HT and COPD) were more prevalent in subjects with thyroid disorder, especially hyperthyroid group. Only CKD was more prevalent in subjects with hypothyroid group. Along with this, Pre- Clinical vitals such as systolic blood pressure (SBP), diastolic blood pressure (DBP), heart rate (HR), respiratory rate (RR) and body temperature (Temp) were also noted. However, no striking difference was observed among the three groups (Fig 2).

![Fig 2](https://example.com/fig2.png)

Figure 2. Pre-clinical vitals of the subjects in three groups

In all the groups, peak lactate levels were observed immediately post-surgery (0 hr) and gradually declined later at 24 hours (Fig 3). A cyclic pattern was observed in all the three groups. Mean preoperative, postoperative lactate levels and rise in blood lactate level (Δ lactate (postoperative-preoperative) are summarized in Table 3. Mean post-operative lactate level and Δ lactate were significantly low in euthyroid group (p-value hyper/hypo Vs Euthy<0.001). Hyperlactatemia is elevated lactate level [blood lactate level ≥ 2.5 mmol/l. Lactic acidosis is defined as blood lactate level ≥ 5.0 mmol/l along with pH<7.35.

![Fig 3](https://example.com/fig3.png)

Figure 3. Variations in the lactate levels of the three group’s pre/post-surgery scenario
Parameter  | Hypo (202) | Hyper (28) | Euthy (330) | P hypo vs euthy | P hyper vs euthy | P hypo vs hyper |
--- | --- | --- | --- | --- | --- | --- |
Mean pre_lact | 1.36 ± 0.5 | 1.57 ± 0.7 | 1.51 ± 1.0 | 0.04 | 1 | 1 |
Mean post_lact | 2.00 ± 0.7 | 1.88 ± 0.8 | 1.69 ± 1.0 | 0.0001 | 0.32 | 0.40 |
Δ lactate | 0.63 ± 1.8 | 0.23 ± 0.8 | 0.18 ± 1.0 | 1 | <0.001 | 1 |
Hyperlactaemia n (%) | 97 (48%) | 13 (46.6%) | 104 (31.5%) | 0.0001 | 0.10 | 0.87 |
Lactic acidosis n (%) | 20 (9.9%) | 3 (10.7%) | 9 (2.7%) | 0.0004 | 0.02 | 0.89 |

Table 3. Mean values of pre-operative and post-operative lactate based parameters

Number of subjects with postoperative elevated lactate levels was significantly low in euthyroid as compared to hypothyroid subjects. Occurrence of lactic acidosis was significantly low in the euthyroid group (hypo vs euthy, p= 0.0004, hyper vs euthy, p= 0.02, hyper vs hypo, p=0.89) (Table 3).

The post-operative parameters of the selected subjects from all the three study groups and effect of presence of hyperlactatemia was evaluated on subjects with thyroid disorder. The two study groups were further divided into subjects with and without hyperlactatemia. Post-operative parameters include duration of ICU stay, length of stay in the hospital (LOS), duration of ventilator support and urinary catheter, number of inotropes and their duration. Among the subjects suffering from thyroid disorder, subjects with hyperlactatemia had prolonged ICU stay and LOS, longer duration of ventilator support and urinary catheter usage, higher number of inotropes for longer time period were used for these subjects with hyperlactatemia. Although significant difference in the parameters can be noted among the subjects with thyroid disorders (‘Hypo’ and ‘Hyper’ group), Not very significant difference was noted among the Euthyroid subjects (‘Euthy’ group) (Fig 4, Fig 5 and Fig 6).

**Fig 4.** Post-operative parameters of the ‘Hypo’ group with and without hyperlactatemia

**Fig 5.** Post-operative parameters of the ‘Hyper’ group with and without hyperlactatemia
Post-operative Outcomes (Euthyroid)

Study parameters

Hyperlactatemia   Normal Lactate

Fig6. Post-operative parameter of the ‘Euthy’ group with and without hyperlactatemia

4. CONCLUSION

Some previous studies have shown that hyperlactatemia can be an indicator of adverse outcomes after any major operation. Post-operative outcomes were compared among the three groups (Hypo, Hyper and Euthy). Subjects in the euthyroid group showed better outcomes. This study indicates that either elevated lactate levels or thyroid status can be a predictor of adverse outcomes after CABG. Since pre-clinical were also compared which didn’t not show any significant differences, therefore, we can conclude that presence of hyperlactatemia made the difference. The results of this study conclude that hyperlactatemia can be an early alarm for reporting adverse post-surgery outcomes in subjects undergoing can CABG with thyroid disorder.

5. DISCUSSION

This demonstrated the potential of hyperlactatemia as an early indicator of adverse outcomes in thyroid subjects undergoing coronary artery bypass surgery. A threshold mark of 2mmol/L at 12 hours and raised lactate levels at 6 hours stay in the ICU are considered independent predictors as they have reported increased 30-day mortality. Hyperlactatemia at 6 hours in ICU stay have recorded a 3.3 times higher risk factor after surgery (9). Elevated lactate levels have been often used as a short term as well as long term predictor in cases of trauma (16), critical illness (17) or sepsis (18). But its role as early predictors for thyroid subjects undergoing coronary artery bypass surgery is still a question. Our study results were in synchrony with studies that reported lactate level elevation soon after ICU admission (8, 19, 20). Immediate rise in lactate levels after surgery is reported by various studies (19, 20, 21).

This study shows that the study groups having higher prevalence of hyperlactatemia often had negative outcomes such as prolonged ICU stay and hospitalization, higher use of IABP, longer durations of use of inotropes, longer ventilator support and increased days of urinary catheter use. These observations were also reported by Juneja et al (23). Ranucci and Coworkers and Shinde et al (25) demonstrated that hyperlactatemia during CPB was associated with higher postoperative use of IABP, longer ICU stay and ventilation support. Similar to our study, Sadeghi et al stated that elevated lactate levels in 6 hours after CABG is more likely related to prolonged ICU and hospital stay and it could be used as a marker of a worse postoperative outcome in terms of mortality as well (26). Early elevation in lactate levels (first 6 hours) after heart surgery are associated with higher rates of morbidity and mortality, therefore these are robust biomarkers of negative clinical outcomes (26-30). It was reported that the maximum level of lactate during cardiac surgery after CPB was directly related with a low oxygen delivery, lengthier LOS and ICU-free survival days (30,31). Since, Δlactate was significantly low in euthyroid patients so, groups with poor outcomes had significantly higher rise in the lactate levels. This was in accordance with Jabbari et al (34).

Our results were slightly similar to Vacate et al (35) as they attempted to study hypothyroid as a predictor of surgical outcomes in elderly subjects. They concluded that normal thyroid levels must be maintained pre operatively.at the same time, our study results were different from Weinberg et al (36) who reviewed surgical outcomes in 59 hypothyroid and euthyroid subjects and found no significant difference in the preoperatives parameters and surgical outcomes. This may be due to therapeutic management of thyroid status.

In conclusion, hyperlactatemia can be an early alarm for adverse post-surgery outcomes in subjects undergoing CABG with deranged thyroid status. Early rise in lactate levels are common observation, irrespective of the thyroid status. Hyperlactatemia and lactic acidosis are less prevalent in euthyroid state. Hyperlactatemia is associated with prolonged ICU stay, lengthened hospitalization and use of ventilator and urinary catheter for longer durations. Further investigations may include effect of medication on hyperlactatemia in subjects undergoing CABG

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