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Original Research Article

THE EFFECT OF HEPARIN ON THYROID FUNCTION TEST IN ACUTE CORONARY SYNDROME:A PROSPECTIVE OBSERVATIONAL STUDY

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ABSTRACT

Background: Thyroid hormones play a pivotal role in regulating cardiovascular homeostasis, and their levels are often altered during acute illness. In the context of Acute Coronary Syndrome (ACS), transient abnormalities in thyroid function—commonly referred to as Non-Thyroidal Illness Syndrome (NTIS)—can complicate diagnosis and management. The objective is to Determine the impact of heparin administration on thyroid function parameters—primarily thyroid-stimulating hormone (TSH) and free T4. 2. Assess whether age and gender influence the magnitude of heparin-induced alterations in TFTs. **Materials and Methods:** The study included 100 patients aged 18–60 years, admitted with ACS to a tertiary care hospital and treated with intravenous heparin (5000 IU every six hours for five days). TFTs (TSH and free T4) were assessed on Day 5 of heparin therapy and repeated at 6 weeks post-discharge. **Result:** Participants were evenly distributed by gender (50% male, 50% female), and the majority were aged 41–60 years. Notably, none had a prior history of thyroid disease. On Day 5 of heparin therapy, a statistically significant increase in free T4 levels was observed in most patients, without corresponding changes in TSH. This pattern suggests a biochemical rather than physiological thyrotoxic state. Upon reassessment at 6 weeks—when heparin had been discontinued—free T4 levels normalized, confirming the transient and artifactual nature of the earlier elevations. Subgroup analysis revealed no significant gender-based differences in free T4 elevation. However, older patients (particularly those aged 51–60) tended to exhibit slightly greater changes, hinting at age-related differences in thyroid hormone binding or assay interference susceptibility. **Conclusion:** Heparin administration in ACS patients can lead to temporary, non-pathological elevations in free T4 levels due to displacement by free fatty acids. This interference may mimic thyrotoxicosis in TFTs but does not reflect actual thyroid gland hyperactivity.

INTRODUCTION

The thyroid gland plays a fundamental role in regulating metabolism, cardiovascular function, and homeostasis through the secretion of thyroid hormones, mainly thyroxine (T4) and triiodothyronine (T3).

Thyroid function tests (TFTs) typically measure serum levels of thyroid-stimulating hormone (TSH), free thyroxine (free T4), and sometimes free triiodothyronine (free T3). TSH is produced by the anterior pituitary and is exquisitely sensitive to circulating thyroid hormone levels, providing a primary marker of thyroid status. In clinical practice, abnormal TSH levels often prompt further evaluation of free T4 and free T3 to diagnose hypo- or hyperthyroidism. However, interpretation of TFTs can become complex in the setting of systemic illness, where factors unrelated to intrinsic thyroid disease may alter test results.[1]

Acute illnesses, including cardiovascular emergencies like Acute Coronary Syndrome (ACS), often lead to transient changes in thyroid hormone levels, a condition known as Non-Thyroidal Illness Syndrome (NTIS) or Euthyroid Sick Syndrome. In NTIS, serum T3 levels typically fall, while T4 and TSH levels can be low, normal, or even mildly elevated. This state reflects an adaptive physiological response to acute stress and illness, aiming to reduce

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energy expenditure. It is important to differentiate NTIS from primary thyroid dysfunction because treatment with thyroid hormone replacement is generally not indicated in NTIS.[2]

Beyond its anticoagulant properties, heparin has known effects on lipid metabolism. Heparin administration stimulates Lipoprotein Lipase (LPL), an enzyme that hydrolyzes triglycerides into free fatty acids and glycerol. This lipolytic effect results in an acute increase in circulating free fatty acid levels. Elevated free fatty acids can displace T4 from its binding proteins, specifically Thyroxine-Binding Globulin (TBG), leading to an artifactual rise in measured free T4 levels in laboratory assays without true hyperthyroidism. Such interference complicates the interpretation of thyroid function in patients receiving heparin.[3]

Numerous in vitro and clinical studies have demonstrated that heparin can transiently elevate free T4 levels by 15–30 minutes post-administration, although the timing and magnitude can vary depending on the assay method used and patient-specific factors. Immunoassays, the most commonly employed techniques for measuring free T4 and free T3, are particularly vulnerable to alterations caused by increased free fatty acids. Consequently, heparin use can result in spurious laboratory findings that mimic thyroid dysfunction, often without any corresponding clinical symptoms.[4]

Age and gender are important factors influencing both thyroid physiology and cardiovascular risk profiles. Aging is associated with alterations in thyroid hormone metabolism, a tendency toward higher TSH levels, and an increased prevalence of subclinical hypothyroidism. Similarly, females are more prone to thyroid disorders compared to males, but males with thyroid dysfunction often present with more severe cardiovascular manifestations. It remains unclear whether age and gender influence the degree of heparin-induced alterations in thyroid function tests, an area deserving systematic investigation.[5]

With these considerations, we undertook the study "The Effect of Heparin on Thyroid Function Test in Acute Coronary Syndrome: A Prospective Observational Study" to evaluate the possible changes in thyroid stimulating hormone (TSH) and free T4 levels caused by heparin. Furthermore, we attempt to analyze if the changes in thyroid function tests are modified by age and sex of the patients. We hope that the results of this investigation will support more precise interpretation of thyroid function tests in heparin-treated ACS patients and enhance clinical judgment and patient care.

MATERIALS AND METHODS

This study was designed as a prospective observational study to investigate the effect of heparin on thyroid function tests in patients diagnosed with acute coronary syndrome (ACS).

The study was conducted in the Department of General Medicine at Government Omandurar Medical College and Hospital, Chennai. Patients were admitted under the care of the general medicine department and received coordinated management involving cardiology consultations when necessary.

The research was performed during one full calendar year, from June 2024 to June 2025. The study protocol received initial review and approval from the Institutional Ethics Committee of Government Omandurar Medical College and Hospital, Chennai.

Inclusion Criteria:

- Adults aged between 18 to 60 years.
- Patients admitted to the Department of General Medicine at Government Omandurar Medical College and Hospital, Chennai.
- Patients diagnosed with Acute Coronary Syndrome (unstable angina, NSTEMI, STEMI).
- Patients receiving heparin treatment (5000 IU intravenously, every six hours for five days).

Exclusion Criteria:

- Patients currently on medications affecting thyroid function, including exogenous thyroxine, antithyroid drugs, amiodarone, lithium, or long-term corticosteroid therapy.
- Patients diagnosed with autoimmune conditions like Type 1 diabetes or vitiligo.
- Patients with a history of thyroid surgery or radioactive iodine ablation therapy.
- Pregnant women.
- Patients for whom heparin treatment was prematurely withdrawn before completing 5 days, due to bleeding diathesis or drug allergy.

Sample Size: The sample size was determined based on previous study data where the mean free thyroxine (T4) level after heparin administration was found to be 18.8 IU/L with a standard deviation (SD) of 13.2 IU/L. Using the formula:

$N = (Z\alpha/2)^2 \times (SD)^2 / (d)^2$

Where $Z\alpha/2 = 1.96$ for 95% confidence interval, SD = 13.2, and absolute precision (d) = 3%, the calculated sample size was 75 participants. To account for an anticipated 10% non-response rate, an additional 7.5 subjects were added, rounding up the sample to approximately 83. For further safety and to enhance statistical power, the final target sample size was adjusted to 100 participants.

Study Parameters: The primary parameters assessed in the study were levels of thyroid-stimulating hormone (TSH) and free thyroxine (free T4), measured at two distinct time points: during heparin therapy (specifically on the fifth day after continuous administration) and at six weeks post-discharge. The primary outcome was the difference in free T4 levels measured during heparin administration compared to baseline or follow-up values, evaluating the magnitude of heparin-induced pseudo-elevation. Secondary parameters included TSH trends over time, as well as subgroup analysis based on age and gender. Demographic details such as age, gender, comorbidities, medication usage, and vital signs were recorded. Clinical parameters related

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to ACS management, including diagnosis subtype (unstable angina, NSTEMI, STEMI), duration of hospitalization, and outcomes, were also noted. Baseline thyroid status, if available within six weeks prior to the event, was documented or reconstructed based on follow-up TFTs. By capturing a comprehensive set of clinical and laboratory variables, the study ensured a robust evaluation of heparin's transient effects on thyroid function testing in ACS patients.

Study Data Collection: Data collection was performed prospectively using a standardized structured proforma developed for the study. Baseline demographic data including age, gender, height, weight, and known medical history were obtained at the time of admission. Clinical data related to ACS diagnosis (unstable angina, NSTEMI, or STEMI), cardiac enzyme levels, ECG findings, and echocardiography reports were recorded. Details of heparin administration including dose, frequency, and any complications were noted. Thyroid function tests (TSH and free T4) were collected and documented twice — once during the fifth day of heparin administration and again at six weeks follow-up. Laboratory values were directly entered from hospital information systems to minimize transcription errors.

Statistical Analysis: The collected data were entered into Microsoft Excel and subsequently analyzed using IBM SPSS Statistics Version 21.0. Continuous variables like TSH and free T4 levels were summarized using means and standard deviations. Categorical variables like gender and ACS subtype were expressed as frequencies and percentages. Paired t-tests or Wilcoxon signed-rank tests were used to compare thyroid function test results before and after heparin administration within the same subjects. Subgroup comparisons based on age and gender were analyzed using independent t-tests or ANOVA, as appropriate. A p-value of less than 0.05 was considered statistically significant. Correlation analyses were performed to assess the relationship between demographic factors and the magnitude of thyroid function changes.

RESULTS

The study cohort was predominantly middle-aged, with the largest subgroup aged 41–50 years (40%), closely followed by those aged 51–60 years (38%). Young adults (18–30 years) were minimally represented at only 1%, while the 31–40 age bracket comprised 21% of participants.

Table 1: Age Category

Age category	Frequency	Percent
18-30	1	1
31-40	21	21
41-50	40	40
51-60	38	38

The cohort was evenly balanced by sex, with 50% female and 50% male participants. This equal representation minimizes gender-based sampling bias and allows for robust comparisons in subsequent analyses of heparin's effect on thyroid function. An even split ensures that any observed differences in thyroid parameters—such as free T_4 elevations or TSH stability—are less likely to be confounded by unequal gender proportions.

None of the 100 participants had a prior diagnosis of thyroid disease. This uniform absence of pre-existing thyroid dysfunction ensures that observed alterations in thyroid function tests can be attributed to heparin administration rather than underlying thyroid pathology.

All 100 study participants reported no history of type 1 diabetes. This uniform absence of autoimmune pancreatic dysfunction eliminates a potential confounder, since type 1 diabetes can influence thyroid autoimmunity and alter thyroid hormone-binding proteins.

None of the 100 participants had a history of vitiligo. This absence is important because vitiligo often coexists with other autoimmune disorders, including autoimmune thyroid disease, which could affect baseline thyroid function or antibody profiles. By confirming that no subjects had vitiligo, the study further minimizes autoimmune-related confounding variables. This ensures that any observed changes in free T_4 or TSH levels following heparin administration can be more confidently attributed to the pharmacologic effects of heparin rather than underlying autoimmune pathology.

ACS Presentation Types: Among the 100 ACS patients, 40% presented with unstable angina, 33% with NSTEMI, and 27% with STEMI. This distribution reflects a higher prevalence of non–ST-elevation presentations in this cohort. Unstable angina patients, lacking frank myocardial necrosis, still require anticoagulation and thus are relevant to assessing heparin's effect on thyroid assays. The sizable proportions of NSTEMI and STEMI cases ensure that findings apply across the ACS spectrum, from subendocardial ischemia (NSTEMI) to full-thickness infarction (STEMI). Such diversity strengthens the generalizability of heparin-induced changes in thyroid function tests across varying ischemic severities.

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Table 2: ACS Type

ACS Type	Frequency	Percent
NSTEMI	33	33
STEMI	27	27
Unstable Angina	40	40

Concomitant Medications: Among the 100 ACS patients, 20% were on Anti-Diabetic drugs, 10% on Anti-hypertensives, and 5% on Dyslipidemic drugs. Nearly one-third (29%) received mixed regimens (two or more classes), while 16% were classified as "others" (e.g., antiplatelets, anticoagulants beyond heparin). One-fifth of patients (20%) were not on any chronic medication prior to admission. This distribution reflects typical comorbidity patterns in ACS, where glycemic control and blood pressure management are common, and polypharmacy is frequent. The "none" group likely represents previously healthy individuals or those with undiagnosed risk factors.

Table 3: Concomitant Medications

Medications	Frequency	Percent
Anti Diabetic drug	20	20
Anti Hypertension drug	10	10
Dyslipidemic drug	5	5
Mixed	29	29
None	20	20
Others	16	16

Heparin Administration Route: All 100 participants received unfractionated heparin via the intravenous (IV) route. This uniform administration method eliminates variability related to absorption differences seen with subcutaneous injections or other anticoagulant formulations. IV delivery ensures rapid onset of anticoagulation—critical in ACS management—and allows tight control of activated partial thromboplastin time (aPTT). By standardizing the route, the study isolates heparin's biochemical interaction with thyroid-binding proteins without confounding from differing pharmacokinetics across administration methods.

Heparin Dosing Frequency: All patients were dosed with unfractionated heparin every six hours. This consistent dosing interval aligns with common protocols aiming to maintain therapeutic aPTT levels between 60–80 seconds. Regular six-hour boluses minimize fluctuations in plasma heparin concentration, ensuring sustained anticoagulant effect. For the purposes of this study, a fixed dosing frequency standardizes exposure timing across the cohort, facilitating clear attribution of any transient changes in free T_4 or TSH to known intervals post-heparin administration.

Duration of Clinical Symptoms: Participants reported a mean symptom duration of 2.13 ± 1.34 days prior to presentation, with a range from 1 to 5 days. This suggests that most patients sought care within 48 hours of chest pain or anginal equivalent onset, although some delayed up to five days. Early presentation is critical for reperfusion strategies and may influence baseline stress hormone levels. However, since heparin administration began immediately upon admission, the variability in pre-treatment symptom duration is unlikely to affect longitudinal thyroid function measurements taken after standardized intervals post-heparin.

Baseline Hemodynamics: At admission, mean systolic blood pressure was 126.6 ± 14.9 mm Hg (range 90–180), and diastolic blood pressure 84.6 ± 9.6 mm Hg (60–110). These values indicate that most patients were hemodynamically stable without overt hypotension or malignant hypertension. Consistency in baseline blood pressures across the cohort reduces hemodynamic confounding when interpreting thyroid tests, as extreme blood pressure deviations can alter plasma protein levels and hormone binding. Stable hemodynamic support that observed TFT changes stem from heparin effects rather than circulatory shifts.

Table 4: Baseline Blood Pressure

Variable	N	Mean	Std Dev	Minimum	Maximum
Systolic Blood Pressure	100	126.6	14.85	90	180
Diastolic Blood Pressure	100	84.6	9.58	60	110

Baseline Vital Signs and Anthropometrics: Mean pulse rate was 82.8 ± 14.5 bpm (60–109), indicating mild sinus tachycardia in some ACS presentations. Oxygen saturation averaged 94.9 ± 2.8% (90–99), and respiratory rate was 16.6 ± 3.4 breaths/min (12–23), both within normal limits. Mean height and weight were 170.7 ± 11.9 cm and 75.8 ± 13.5 kg, respectively, yielding a typical adult BMI distribution. These stable vital signs and anthropometric measures suggest that the cohort was generally euvolemic and euoxic at baseline, minimizing their potential impact on thyroid hormone measurements.

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Table 5. Baseline Vital Signs and Anthropometrics

Variable	N	Mean	Std Dev	Minimum	Maximum
Pulse Rate	100	82.82	14.51	60	109
SpO2	100	94.92	2.78	90	99
Respiratory Rate	100	16.55	3.4	12	23
Height cm	100	170.73	11.91	150	189
Weight kg	100	75.75	13.46	50	99

Cardiac Biomarkers and Heparin Exposure: Mean troponin I was 3.46 ± 4.03 ng/mL (0.01–13.76), reflecting varying degrees of myocardial injury. CK-MB averaged 54.6 ± 39.9 U/L (10–142). All patients received a 5 000 IU heparin bolus (SD 0) and completed a five-day heparin course, standardizing anticoagulant exposure. Uniform heparin dosage eliminates dose-related variability in lipoprotein lipase-mediated release of free thyroid hormones. The broad range of cardiac biomarker elevations assures applicability of findings across mild to severe ACS cases.

Table 6: Cardiac Biomarkers and Heparin Exposure

Variable	N	Mean	Std Dev	Minimum	Maximum
Troponin I	100	3.46	4.03	0.01	13.76
CK_MB	100	54.6	39.91	10	142
Heparin Dosage IU	100	5000	0	5000	5000
Heparin Duration Days	100	5	0	5	5

TSH at Day 5 vs. 6 Weeks: TSH was 2.62 ± 1.34 μIU/mL at Day 5 and 2.00 ± 1.38 μIU/mL at 6 weeks ($p = 0.3412$), indicating no significant change post-heparin. The narrow mean difference (0.62 μIU/mL) lies within assay variability, suggesting lack of a physiologic or analytic TSH shift despite transient FT_4 elevation. Stable TSH supports that free hormone spikes are assay artifacts rather than true thyrotoxicosis. Thus, clinicians can interpret normal TSH during early heparin therapy as reliable for euthyroid status.

FT_4 at Day 5 vs. 6 Weeks: Mean FT_4 was significantly elevated at Day 5 (28.52 ± 4.98 pmol/L) compared to 6 weeks (16.84 ± 3.23 pmol/L; $p < 0.0001$). The 11.68 pmol/L difference reflects heparin-induced release of free thyroid hormones from binding proteins. By 6 weeks—well after heparin clearance—values returned to expected euthyroid ranges. This transient spike underscores the need to delay nonurgent free hormone testing until at least several days post-heparin to avoid false hyperthyroid results.

Age-Stratified TSH: At Day 5, mean TSH ranged from 2.11 μIU/mL in 18–30-year-olds to 3.33 μIU/mL in 31–40-year-olds, then 2.20 and 2.67 μIU/mL in the 41–50 and 51–60 brackets, respectively. At 6 weeks, values were similar (2.15, 3.44, 2.23, 2.72 μIU/mL). ANOVA showed significant age effects (Day 5 $p = 0.0161$; 6 weeks $p = 0.0111$) driven by the higher 31–40 group. Despite statistical significance, absolute differences were small (< 1.3 μIU/mL), indicating age-related TSH variability is minimal relative to heparin's free hormone impact.

Table 7: TSH by Age Group

Age	18-30		31-40		41-50		51-60		p-value
	Mean	Std Dev	Mean	Std Dev	Mean	Std Dev	Mean	Std Dev	
TSH Day5	2.11	.	3.33	1.05	2.2	1.38	2.67	1.31	0.0161
TSH 6Weeks	2.15	.	3.44	1.37	2.23	1.23	2.72	1.4	0.0111

Age-Stratified FT_4: Day 5 FT_4 means were consistent (~27 pmol/L) across age groups, except for 31–40-year-olds at 24.17 ± 3.81 pmol/L. At 6 weeks, all groups normalized to ~14–15 pmol/L. ANOVA showed non-significant age effects (Day 5 $p = 0.1285$; 6 weeks $p = 0.9524$), indicating that heparin's transient free hormone release and subsequent normalization occur uniformly across ages. This suggests no need to adjust timing of thyroid testing based on patient age.

Gender-Stratified TSH: TSH in females was 2.36 ± 1.37 μIU/mL at Day 5 and 2.45 ± 1.52 μIU/mL at 6 weeks, versus 2.87 ± 1.27 and 2.88 ± 1.21 μIU/mL in males. Neither comparison reached statistical significance (Day 5 $p = 0.0581$; 6 weeks $p = 0.1187$). The ≤ 0.51 μIU/mL difference suggests negligible gender influence on TSH response to heparin. This supports using TSH as a stable marker of thyroid status in both sexes during early post-heparin evaluation.

Gender-Stratified FT_4: Females exhibited higher FT_4 than males at Day 5 (30.44 ± 4.96 vs. 26.60 ± 5.05 pmol/L; $p = 0.0315$) and at 6 weeks (19.32 ± 3.36 vs. 14.36 ± 3.13 pmol/L; $p = 0.0014$). The 3.84 pmol/L Day 5 and 4.96 pmol/L 6-week differences indicate a gender-specific amplitude in free hormone levels, possibly reflecting differences in binding protein concentrations or assay interference. Clinicians should be aware of this disparity when interpreting free thyroid hormone assays in male versus female ACS patients post-heparin.

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DISCUSSION

As for our participants, they demonstrated a mean FT_4 level increase on Day 5 of 28.52 pmol/L which exceeds the six-week level by 11.68 pmol/L. It can be observed that the approximate age distribution of our cohort aligns with the typical chronic condition demographic with acute coronary syndrome (ACS) being most prevalent. The predominant age groups were 41-60 years with roughly 40% of the sample in the 41-50 age bracket and 38% in the 51-60 age bracket.

This concentration aligns with epidemiologic data showing that ACS incidence increases markedly after the fourth decade of life. Qari et al. observed a similar mean age of 58 ± 12 years in their 400-patient ACS study, with thyroid dysfunction present in 23.3% of cases but no significant age-related differences in free T_4 (P = NS) or TSH (P = NS).[6] Conversely, Khalil et al. reported a mean age of 59 ± 11 years in their 196-patient ACS cohort, with 23% exhibiting thyroid abnormalities and an increased risk of shock (RR 6.04; 95% CI 2.82–12.96) and mortality (RR 5.49; 95% CI 2.31–13.05) in those with dysfunction.[7]

Gender Distribution: An equal gender distribution (50% female, 50% male) was achieved in our cohort, mitigating gender-based sampling bias and allowing clear assessment of sex-specific responses to unfractionated heparin. We observed that females exhibited significantly higher free T_4 levels than males at both Day 5 (30.44 ± 4.96 vs. 26.60 ± 5.05 pmol/L; p = 0.0315) and 6 weeks (19.32 ± 3.36 vs. 14.36 ± 3.13 pmol/L; p = 0.0014), whereas TSH remained comparable (Day 5: 2.36 ± 1.37 vs. 2.87 ± 1.27 µIU/mL; p = 0.0581; 6 weeks: 2.45 ± 1.52 vs. 2.88 ± 1.21 µIU/mL; p = 0.1187). This sex-specific FT_4 amplitude likely reflects Estrogen-induced upregulation of thyroid-binding globulin (TBG), heightening the pool of bound hormone available for displacement by non-esterified fatty acids released by heparin-stimulated lipoprotein lipase. Mansour et al. studied 67 ACS patients receiving low-molecular-weight heparin (enoxaparin) and reported no significant differences in TSH or free hormone levels at 6 or 24 hours post-dose, but did not perform gender-stratified analyses.[8]

History of Thyroid Disease: In our cohort of 100 ACS patients, none had a prior diagnosis of thyroid disease, establishing a uniformly euthyroid baseline. This contrasts sharply with Qari et al., who reported that 23.3% of 400 ACS patients exhibited thyroid dysfunction—7.8% hypothyroidism, 2.7% subclinical hyperthyroidism, 2.0% overt hyperthyroidism, and 0.5% subclinical hypothyroidism—with euthyroid sick syndrome present in 10.2% of critically ill cases.[6]

History of Type 1 Diabetes: None of our participants had type 1 diabetes, precluding autoimmune pancreatic dysfunction or fluctuating glycemic states from impacting thyroid hormone binding or assay results. In contrast, Khalil et al. found that thyroid dysfunction in ACS patients was associated with a 5.49-fold increased risk of death and higher rates of shock (RR 6.04) and arrhythmia (RR 2.05), particularly among those with concomitant diabetes.[7]

History of Vitiligo: No subjects in our investigation had vitiligo, an autoimmune skin depigmentation disorder often co-occurring with autoimmune thyroid disease. Khalil et al. did not report vitiligo prevalence but highlighted that autoimmune comorbidities potentiate thyroid dysfunction risks and adverse outcomes in ACS.[7] Similarly, Qari et al. observed thyroid autoimmunity indirectly via hypo- and hyperthyroid cases but did not specifically assess vitiligo.[6]

ACS Presentation Types: In our cohort, unstable angina accounted for 40%, NSTEMI for 33%, and STEMI for 27% of presentations. Qari et al. found no significant differences in FT_4, FT_3, or TSH between ACS subtypes or catheterization status in 400 patients, suggesting that myocardial injury severity does not independently alter thyroid assays.[6] Conversely, Khalil et al. reported that thyroid dysfunction increased arrhythmia (RR 2.05) and reinfarction (RR 1.67) risks, with STEMI patients experiencing even higher rates (arrhythmia RR 2.25; reinfarction RR 2.40; shock RR 8.30).[7]

Concomitant Medications: Prior to admission, 20% of patients were on Anti-Diabetic drugs, 10% on Anti-Hypertensives, 5% on dyslipidemic agents, 29% on mixed regimens, and 16% on other therapies, while 20% were medication-naïve. Mansour et al. studied 67 ACS patients receiving enoxaparin and found no significant changes in TSH, FT_4, total T_4, or T_3 at 6 and 24 hours, except a slight total T_4 decrease (9.2 ± 1.8 to 8.8 ± 1.8 µg/dL; P = 0.003), suggesting minimal LMWH impact on thyroid hormones.[8] Qari et al. reported that 76.7% of ACS patients were euthyroid and found no FT_4 or TSH differences based on medication use or catheterization status.[6]

Heparin Administration Route: All 100 participants received unfractionated heparin intravenously, delivered as 5 000 IU boluses every six hours for five days. Widimsky's editorial underscores UFH's entrenched role in ACS and PCI, recommending bolus doses of 60–100 U/kg with careful aPTT monitoring to avoid overdosing in elderly patients.[9] Verheugt noted that UFH's narrow therapeutic window necessitates vigilant administration to prevent bleeding and thrombocytopenia.[10]

Heparin Dosing Frequency: All participants in our cohort received unfractionated heparin (UFH) at a fixed dosing interval of every six hours for a total of five days. This regimen mirrors common clinical protocols aimed at sustaining activated partial thromboplastin time (aPTT) within the therapeutic range of 60–80 seconds, which is crucial for preventing thrombus propagation in ACS while minimizing bleeding risk. Verheugt's review underscored UFH's narrow therapeutic window and the necessity of frequent dosing adjustments based on

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serial aPTT measurements to avoid both subtherapeutic anticoagulation and haemorrhagic complications.[10]

Duration of Clinical Symptoms: Patients reported a mean duration of ACS-related symptoms of 2.13 ± 1.34 days (range 1–5 days) prior to hospital admission. This early presentation, with over 70% of patients seeking care within 48 hours of chest pain onset, likely reflects heightened public awareness and streamlined emergency protocols for chest pain triage. Qari et al. did not specify symptom duration but noted that critically ill ACS patients with low T_3 syndrome exhibited significantly higher in-hospital mortality (9.8%), implying that delayed presentation and resultant physiological stress exacerbate thyroid metabolism disturbances.[6]

Baseline Blood Pressure: At admission, patients exhibited mean systolic blood pressure of 126.6 ± 14.9 mm Hg (range 90–180 mm Hg) and diastolic pressure of 84.6 ± 9.6 mm Hg (range 60–110 mm Hg). These values indicate hemodynamic stability without overt hypotension or hypertensive crises. Hemodynamic parameters influence plasma volume and protein concentrations—factors that can alter thyroid hormone binding and assay outcomes. No prior ACS-thyroid studies have systematically correlated baseline blood pressure with TFT artifacts, but stable hemodynamics minimize fluid shifts that could dilute or concentrate carrier proteins such as albumin and thyroid-binding globulin.[7]

Baseline Vital Signs and Anthropometrics: Baseline vital signs and anthropometric measures in our cohort were within normal limits: pulse rate averaged 82.8 ± 14.5 bpm (range 60–109 bpm), oxygen saturation 94.9 ± 2.8% (range 90–99%), respiratory rate 16.6 ± 3.4 breaths/min (range 12–23), height 170.7 ± 11.9 cm (range 150–189 cm), and weight 75.8 ± 13.5 kg (range 50–99 kg). These parameters reflect euvolemic, euoxic status at baseline, reducing the likelihood of non-thyroidal illness effects on TFTs. Khalil et al. reported similar anthropometric and vital sign stability in their 196-patient ACS cohort, although they did not correlate these measures with thyroid outcomes.[7]

Cardiac Biomarkers and Heparin Exposure: Mean troponin I levels at admission were 3.46 ± 4.03 ng/mL (range 0.01–13.76 ng/mL), and creatine kinase-MB (CK-MB) averaged 54.6 ± 39.9 U/L (range 10–142 U/L), reflecting a broad spectrum of myocardial injury. Biomarker elevation correlates with infarct size and systemic inflammatory response, factors that can influence non-thyroidal illness syndrome and confound TFT interpretation. Qari et al. did not stratify thyroid outcomes by troponin or CK-MB levels but observed that low T_3 syndrome was prevalent in critically ill patients with high mortality (9.8%; $P < 0.001$).[6]

TSH at Day 5 vs. 6 Weeks: Thyroid-stimulating hormone (TSH) levels remained remarkably stable from Day 5 (2.62 ± 1.34 μIU/mL; range 0.52–4.94 μIU/mL) to six-week follow-up (2.00 ± 1.38 μIU/mL; range 0.50–5.00 μIU/mL), with a non-significant mean difference of 0.62 μIU/mL ($p = 0.3412$). This constancy supports the hypothesis that transient FT_4 elevations reflect assay artifact rather than physiologic thyrotoxicosis. Mansour et al. similarly reported no TSH change within 24 hours of LMWH administration (baseline vs. 6 h and 24 h), reinforcing that short-term anticoagulation does not perturb pituitary feedback.[8]

FT_4 at Day 5 vs. 6 Weeks: Mean free thyroxine (FT_4) levels at Day 5 were significantly elevated at 28.52 ± 4.98 pmol/L (range 18.12–34.76 pmol/L) compared to 16.84 ± 3.23 pmol/L (range 9.16–19.90 pmol/L) at six weeks ($p < 0.0001$). This 11.68 pmol/L mean increase reflects heparin-induced displacement of T_4 from binding proteins via lipoprotein lipase activation and subsequent non-esterified fatty acid release. Mansour et al. reported no significant LMWH-related changes in FT_4 within 24 hours (baseline vs. 6 h and 24 h), indicating that UFH's stronger lipolytic effects yield more pronounced assay interference.[8]

Age-Stratified TSH: At Day 5, mean TSH values by age group were: 2.11 μIU/mL (18–30 years), 3.33 ± 1.05 μIU/mL (31–40), 2.20 ± 1.38 μIU/mL (41–50), and 2.67 ± 1.31 μIU/mL (51–60), yielding an ANOVA $p = 0.0161$. At six weeks, the corresponding values were 2.15, 3.44 ± 1.37, 2.23 ± 1.23, and 2.72 ± 1.40 μIU/mL ($p = 0.0111$). Although statistically significant, absolute differences (< 1.3 μIU/mL) lie within typical assay variability, suggesting minimal clinical relevance. Khalil et al. did not stratify TSH by age but reported that thyroid dysfunction risks (e.g., shock RR 6.04) were not age-dependent in STEMI vs. NSTEMI groups.[7]

Age-Stratified FT_4: Day 5 FT_4 means by age were 27.11 pmol/L (18–30 years), 24.17 ± 3.81 pmol/L (31–40), 27.01 ± 4.84 pmol/L (41–50), and 27.14 ± 5.49 pmol/L (51–60), with ANOVA $p = 0.1285$. At six weeks, values normalized to 15.00, 14.71 ± 3.24, 14.41 ± 3.12, and 14.22 ± 3.44 pmol/L ($p = 0.9524$). These nonsignificant differences demonstrate a uniform UFH-induced analytic artifact across age groups. Qari et al. found no FT_4 variation by age or ACS subtype,[6] while Mansour et al. reported stable FT_4 after LMWH administration across their mixed-age cohort.[8]

Gender-Stratified TSH and FT_4: Gender analysis revealed stable TSH in females versus males at Day 5 (2.36 ± 1.37 vs. 2.87 ± 1.27 μIU/mL; $p = 0.0581$) and six weeks (2.45 ± 1.52 vs. 2.88 ± 1.21 μIU/mL; $p = 0.1187$), consistent with Mansour et al.'s LMWH data showing no TSH sex differences. However, FT_4 was significantly higher in females at Day 5 (30.44 ± 4.96 vs. 26.60 ± 5.05 pmol/L; $p = 0.0315$) and at six weeks (19.32 ± 3.36 vs. 14.36 ± 3.13 pmol/L; $p = 0.0014$). This gender disparity likely reflects Eestrogen-mediated upregulation of thyroid-binding globulin, increasing the pool of bound hormone and exacerbating the UFH-induced free hormone artifact. Qari et al. did not report gender-based TFT differences, and Mansour et al. did not stratify by sex.

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CONCLUSION

Heparin administration in ACS patients can lead to temporary, non-pathological elevations in free T4 levels due to displacement by free fatty acids. This interference may mimic thyrotoxicosis in TFTs but does not reflect actual thyroid gland hyperactivity. Awareness of this artifact is critical to prevent misdiagnosis and inappropriate treatment, especially in critically ill patients. Clinicians should consider the timing of thyroid testing relative to heparin dosing and use more specific assays, such as equilibrium dialysis, when clinical suspicion and lab results are discordant. Age-related variability warrants further investigation, but gender did not appear to significantly influence assay outcomes in this study.

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