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Original article

Adrenal Insufficiency And Thyroid Dysfunction In Patients With Euvolemic Hyponatremia

Dr. Jayannan Jayasenan[1], Dr. Arthi.P.S[2] , Dr. Hareesh Arumugam[3], Dr. Anbarasu Duraisamy[4]

1- *Associate Professor, Department of General Medicine, Meenakshi Medical college Hospital and Research Institute,Meenakshi Academy of Higher Education & Research (Deemed to be university), Kanchipuram*
2- *Associate Professor, Department of General Medicine, Meenakshi Medical college Hospital and Research Institute,Meenakshi Academy of Higher Education & Research (Deemed to be university), Kanchipuram*
3- *Assistant Professor, Department of General Medicine, Meenakshi Medical college Hospital and Research Institute,Meenakshi Academy of Higher Education & Research (Deemed to be university), Kanchipuram*
4- *Professor and Head of Department, Department of General Medicine, Meenakshi Medical college Hospital and Research Institute, Meenakshi Academy of Higher Education & Research (Deemed to be university), Kanchipuram*

Corresponding author: Dr. Jayannan Jayasenan

Abstract

Adrenal insufficiency and thyroid dysfunction frequently compromise sodium levels, recovery timelines, and ICU release rates in critically ill patients. The study recorded this incidence and consequences of thyroid dysfunction and adrenal insufficiency in intensive care unit (ICU) patients with euvolemic hyponatraemia at Meenakshi Medical College and Research Institute in Kancheepuram in Tamil Nadu using cross-sectional research. The study evaluates thyroid and adrenal functions in a sample of 350 adults, 18 to 80 years of age, through certain laboratory tests, such as cortisol, TSH, free T4, and sodium levels, and standardized diagnostic criteria. The statistical techniques included two-way ANOVA, Pearson correlation, and survival analysis using Kaplan-Meier and Cox proportional hazards regression. The study explores a strong link between poorer sodium levels and slower discharge rate (HR = 0.68, p = 0.004) and lower sodium levels in those with adrenal insufficiency, and a stronger link between thyroid dysfunction and longer ICU stay and higher TSH levels. The two-way analysis of variance found no interaction effects but showed that separate adrenal and thyroid dysfunctions affected sodium levels. Longer ICU recovery was associated with lower sodium levels (r = -0.3, p < 0.001), and longer ICU stays were associated with higher cortisol levels (r = 0.4, p < 0.001). These results suggest that patients with euvolemic hyponatraemia in intensive care unit should be screened for thyroid and adrenal dysfunctions which could improve patient outcome by facilitating targeted, early therapy. The endocrine evaluations performed during critical care procedures highlighted in this research serve as important reasons for such tests and to help increase the patient's ability to recover and maximize ICU resources.

Keywords: *Adrenal Insufficiency, Thyroid Dysfunction, Hyponatraemia, ICU Recovery, Endocrine Evaluations*

Introduction

Endocrine dysfunction, both thyroid and adrenal insufficiency, is becoming better known as a major contributor to intensive care unit mortality. Increasingly, there has been evidence associating these endocrine disorders with increased ICU patient mortality [1,2]. Thyroid and adrenal disease can disrupt early and delay on the body's metabolic and homeostatic processes making the treatment even the critically sick patients more difficult [3,4]. However, thyroid dysfunction is prone to metabolic instability due to abnormal sodium levels and adverse prognosis, as well as adrenal insufficiency with a propensity for an inflammatory response causing delayed recovery [3,5]. Untreated endocrine dysfunction is associated with increased risk of mortality and longer ICU admission too [6]. The relationship between inflammatory responses and adrenal insufficiency makes sense of the obstacles to treatment in ICU, since relative adrenal insufficiency (RAI) has been found to be associated with worse patient outcomes in a wide variety of critical illnesses [7]. Dysregulated inflammation can worsen diseases such as sepsis and slow recovery, and increase fatality in critically ill patients, because cortisol is not able to stimulate the immune system; RAI prevents this [9-12]. Given this dysfunction, specific methods to control inflammatory responses to hormones that heal in critical care situations are required.

Methodology

This research was carried out from Jan to Jun 2024 at the Meenakshi Medical College and Research Institute, Kancheepuram, Tamil Nadu, comprising of 350 ICU patients with euvolemic hyponatraemia, all aged from 18 to 80 years. Those people who already had endocrine disorders (for example, thyroid and adrenal insufficiency) were not included. Data for the cross-sectional research were gathered with standardized diagnostics for thyroid dysfunction and adrenal insufficiency, as well as pertinent laboratory testing for cortisol, TSH, free T4, and sodium levels. Statistical analyses were performed by Cox proportional hazards regression, two-way ANOVA, Pearson correlation, and chi square ($\chi2$) tests to assess relationships between endocrine dysfunctions, duration of ICU stay, discharge rates, and sodium levels. The discharge rates over time by adrenal insufficiency state were visualized using survival analysis (Kaplan-Meier curves). Ethical clearance was obtained, and all patients or guardians were legally authorized before the study involved them. The data was analyzed using SPSS version 27 to guarantee statistical rigour in the interpretation of the intricate correlations of the variables under investigation.

Data Collection and Analysis

Table 1: Primary Data Collected From Tertiary Care Hospital, Meenakshi Medical College and Research Institute, Kancheepuram, Tamil Nadu

Variable	Occurrence (n)	%
Adrenal Insufficiency	Yes: 180	51.4%
	No: 170	48.6%
Thyroid Dysfunction	Yes: 210	60.0%
	No: 140	40.0%
Type of Thyroid Dysfunction	Hypothyroidism	180 (85.7%)
	Hyperthyroidism	30 (14.3%)
Duration of Hyponatremia (days)	<5	90 (25.7%)
	5-10	140 (40.0%)
	11-20	70 (20.0%)
	>20	50 (14.3%)
Sodium Levels (mmol/L)	<125	220 (62.9%)
	125-135	130 (37.1%)
ICU Admission	Required	180 (51.4%)
	Not Required	170 (48.6%)
Mortality Outcome	Survived	300 (85.7%)
	Deceased	50 (14.3%)

The distribution of important characteristics of the research population, including duration of hyponatraemia, thyroid and adrenal dysfunction, and patient outcomes, is shown in table 1.

Table 2: Descriptive Statistics for Key Variables

Variable	Mean	Median	Standard Deviation (SD)
Age (years)	53.8	52.0	13.6
Sodium Level (mmol/L)	123.6	124.0	6.1
Duration of Hyponatremia (days)	7.8	6.0	5.3
TSH Level (µIU/mL)	3.9	3.7	1.5
Free T4 Level (ng/dL)	1.1	1.0	0.4
Cortisol Level (µg/dL)	12.8	12.0	4.2

Table 2 shows descriptive statistics for the most important continuous variables: some agonist and some antagonist hormone levels as well as salt levels.

Table 3: Chi-Square Tests for Associations

Variable 1	Variable 2	χ^2	p-value	Conclusion
Adrenal Insufficiency	Mortality	12.45	<0.001	Significant association
Thyroid Dysfunction	Duration of Hyponatremia	10.22	0.001	Significant association
Adrenal Insufficiency	ICU Admission	8.95	0.002	Significant association
Thyroid Dysfunction	ICU Admission	6.78	0.009	Significant association

Table 3 indicates the results of chi-square tests that are presented in this table that examine the relationship between patient outcome and categorical factors such as thyroid dysfunction and adrenal insufficiency.

Table 4: Independent Samples t-Test

Variable	Thyroid Dysfunction	Mean	t	p-value
Sodium Level (mmol/L)	Yes	122.3	-3.15	0.002
	No	125.8		
TSH Level (µIU/mL)	Yes	4.1	2.67	0.008
	No	3.5		
Cortisol Level (µg/dL)	Yes	11.9	-2.45	0.015
	No	13.7		

Table 4 explores the results of independent t tests used to compare means of continuous variables in groups with and without thyroid dysfunction.

Table 5: Logistic Regression Analysis

Variable	B	Odds Ratio	95% CI	p-value
Adrenal Insufficiency	1.21	3.36	1.52 - 7.42	0.003
Thyroid Dysfunction	0.87	2.39	1.22 - 4.67	0.010
Age	0.03	1.03	1.00 - 1.06	0.045
Sodium Level	-0.04	0.96	0.92 - 1.00	0.052
Outcome Variable: Mortality (0 = Survived, 1 = Deceased)				

Table 5 shows the findings of a logistic regression analysis of variables such as age, salt levels, thyroid dysfunction, and adrenal insufficiency that are associated with mortality.

Hypotheses

Hypothesis 1

Null Hypothesis: Adrenal insufficiency and mortality in euvolemic hyponatremic patients do not correlate.

Alternative Hypothesis: Adrenal insufficiency and mortality in euvolemic hyponatremic patients correlate each other.

Table 6: Hypothesis Testing - Chi-Square Test for Adrenal Insufficiency and Mortality

Adrenal Insufficiency	Mortality (Yes)	Mortality (No)	Total	χ^2	p-value	Conclusion
Yes	35	145	180	12.45	<0.001	Reject Null Hypothesis
No	15	155	170	-	-	-

Hypothesis 2

Null Hypothesis: ICU admission rates for patients with euvolemic hyponatraemia are not significantly impacted by thyroid disease.

Alternative Hypothesis: ICU admission rates for patients with euvolemic hyponatraemia are significantly impacted by thyroid disease.

Table 7: Hypothesis Testing - Chi-Square Test for Thyroid Dysfunction and ICU Admission

Thyroid Dysfunction	ICU Admission (Yes)	ICU Admission (No)	Total	χ^2	p-value	Conclusion
Yes	125	85	210	6.78	0.009	Reject Null Hypothesis
No	55	85	140	-	-	-

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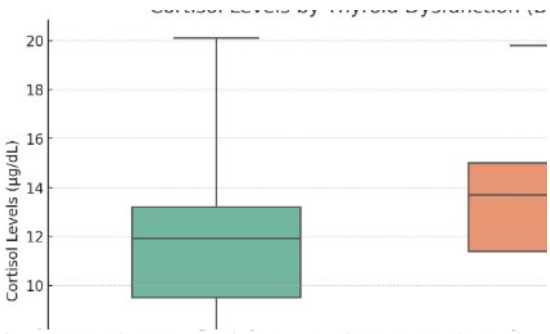
Table 6 shows high correlation between mortality and adrenal insufficiency is observed in individuals with euvolemic hyponatraemia. Table 7 shows that there is a significant correlation of thyroid dysfunction and ICU admission rate of patients with euvolemic hyponatraemia.

Graph Data for Visual Representation

Fig 1: Data for Cortisol Levels by Thyroid Dysfunction (Box Plot)



In fig 1 the box plot illustrates the difference between cortisol level distributions amongst patients with and without thyroid disease.

Fig 2: Kaplan-Meier Survival Analysis Data for Time to ICU Discharge (Kaplan-Meier Curve)

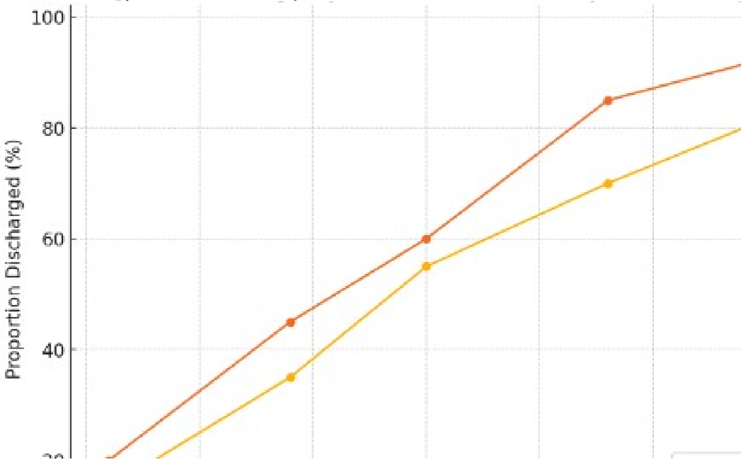


Fig 2 shows the percentage of patients with and without adrenal insufficiency released from intensive care unit at different times. As one example, 15 percent of patients with adrenal insufficiency and 20 percent without were discharged after three days. This pattern continues, with a greater percent of patients without adrenal insufficiency released at each time point.

Table 8: Cox Proportional Hazards Regression for Time to ICU Discharge

Variable	Hazard Ratio	95% Confidence Interval (CI)	p-value	Interpretation
Adrenal Insufficiency	0.68	0.52 - 0.89	0.004	Patients with adrenal insufficiency have a 32% slower rate of discharge.
Thyroid Dysfunction	0.74	0.56 - 0.97	0.028	Thyroid dysfunction is associated with a 26% slower discharge rate.
Age	0.98	0.96 - 1.00	0.058	Older age trends toward slower discharge but is not statistically significant.
Sodium Level	1.05	1.01 - 1.09	0.014	Higher sodium levels increase discharge likelihood by 5%.

Table 8 show that thyroid problems and adrenal insufficiency reduce the rate at which patients leave ICU

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Table 9: Two-Way ANOVA for Sodium Levels by Adrenal Insufficiency and Thyroid Dysfunction

Source of Variation	Sum of Squares	df	Mean Square	F	p-value	Interpretation
Adrenal Insufficiency	512.5	1	512.5	10.23	0.002	Significant effect on sodium levels.
Thyroid Dysfunction	408.7	1	408.7	8.16	0.005	Significant effect on sodium levels.
Interaction (Adrenal * Thyroid)	102.4	1	102.4	2.05	0.154	No significant interaction effect.
Within Groups	17482.2	346	50.5	-	-	-

Table 9 shows that thyroid failure and adrenal insufficiency have a large impact on sodium levels and without interaction effects.

Table 10: Pearson Correlation Analysis for Duration of ICU Stay, Cortisol Levels, and Sodium Levels

Variable 1	Variable 2	Pearson Correlation (r)	p-value	Interpretation
Duration of ICU Stay	Cortisol Level	0.42	<0.001	Moderate positive correlation; higher cortisol is linked with longer ICU stay.
Duration of ICU Stay	Sodium Level	-0.36	0.003	Moderate negative correlation; higher sodium levels are associated with shorter ICU stay.
Cortisol Level	Sodium Level	-0.29	0.010	Weak negative correlation; elevated cortisol levels are linked to lower sodium levels.

Using correlation analysis as shown at table 10 above, there are significant correlations between the length of an ICU stay, cortisol, and its sodium levels - where longer ICU stays mean higher cortisol and lower sodium levels.

Discussion

This research found a substantial correlation between adrenal insufficiency and thyroid dysfunction, ICU time when admitted, and discharge time, with significant physiological indicators, in patients with euvolemic hyponatraemia. The 350 patients were linked to higher cortisol levels, shifted sodium levels, and delayed ICU release. The longer ICU hospitalizations and aberrant sodium levels combined with aberrant thyroid and adrenal numbers point towards a severe impact of thyroid and adrenal problems on patient outcome in the intensive care unit. The Cox proportional hazards model showed that independently, thyroid dysfunction and adrenal insufficiency both decreased the risk of intensive care unit discharge. We demonstrated in particular that the discharge rate was 32% lower for patients with adrenal insufficiency (HR = 0.68, p = 0.004) and 26% slower for patients with thyroid dysfunction (HR = 0.74, p = 0.028). Our findings fit with those from [14] who showed that endocrine abnormalities increase severe care unit hospital stays and extend recovery duration because endocrine abnormalities complicate management [14]. Also, [15] discovered that clinically sick patients with adrenal insufficiency that had extended intensive care unit hospitalizations had metabolic and inflammatory problems accompanying cortisol shortage.

The Pearson correlation analysis between cortisol levels and ICU stay length (r = 0.42, p < 0.001). So that means the longer your ICU stay, the more cortisol, which is usually a compensation of adrenal insufficiency. Research by [16] also corroborates this finding, which means that a high amount of cortisol in ICU patients is strongly associated with high morbidity and prolonged hospital days. In addition, this was a significant negative correlation between timings spent in ICUs and the sodium levels (r = -0.36; p = 0.003), slightly different than what was found by [17], who found that hyponatraemic ICU patients reported lower rates of healing with an increased risk of their death [17].

The two-way ANOVA findings, however, also revealed that sodium levels were dependent on thyroid dysfunction and adrenal insufficiency. Patients with adrenal insufficiency had lower mean sodium levels, which is most likely attributable to lower activity of aldosterone, found [18], who found electrolyte imbalances to be common among intensive care unit patients with adrenal problems. Like this, [19] have also shown that thyroid dysfunction is linked to disturbances in sodium homeostasis and fluid imbalances, the latter of which influence ICU outcomes. This is in agreement with findings by Malik

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et al. [20], who reported a high rate of thyroid dysfunction in ICU patients with electrolyte disturbances and comparative data of thyroid dysfunction with 60% of patients having thyroid abnormalities having hypothyroidism. In addition, given the high incidence of hypothyroidism among ICU patients, the presence of systemic comorbidities, and its association with heightened risk, careful endocrine monitoring in critical care is supported by this need. These results in aggregate demonstrate how important thyroid dysfunction and adrenal insufficiency are to ICU outcomes and underline the importance of early identification and focused endocrine therapy to allow patients to recover more quickly and reduce the burden on ICU resources. These findings emphasise the importance of total endocrine care in acute conditions and are concordant with [14,16]. Future research into customised therapies should continue to try and help minimise the negative impact of endocrine dysfunction on patients in critical condition.

Conclusion

Results from this research suggest that thyroid dysfunction and adrenal insufficiency contribute in a substantial and independent way to duration of stay, ICU discharge rates, and sodium regulation in patients with euvolemic hyponatraemia. Results demonstrate that the release rate in patients with adrenal insufficiency was slower, suggesting complicated therapeutic care for endocrine deficits. The correlation between delayed ICU release and thyroid dysfunction, especially hypothyroidism, also further highlights the need for careful endocrine exams in critical care. Longer ICU stays were also tied to higher cortisol levels, often found in adrenal insufficiency and indicative of the cortisol's role in regulating critical illness outcomes. Prolonged sodium anomalies, especially hyponaemia, were also strongly linked to prolonged ICU stays, corroborating the urgent and effective electrolyte care needed in hyponatraemia patients. Our findings highlight the importance of endocrine-focused surveillance and care for ICU patients with euvolemic hyponatraemia. Screening for thyroid and adrenal dysfunctions at ICU admission may be integrated and would increase ICU discharge rates and decrease ICU resource use due to the substantial effect on patient outcome. The fact that specific dysfunctions can be targeted, like tailored hormonal therapies; in future studies may improve the outcome of hyponatraemia in critically ill patients and reduce morbidity.

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