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Navigating Thyroid Crises: A Nationwide Analysis of the Weekend Effect and Mortality Trends in Myxedema Coma (2016-2020)

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RESEARCH ARTICLE

Navigating Thyroid Crises: A Nationwide Analysis of the Weekend Effect and Mortality Trends in Myxedema Coma (2016–2020)☆

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Abstract

Our objective was to utilize the National Inpatient Sample (NIS) database for analyzing the outcomes of myxedema coma based on the day of admission and explore five-year mortality trends. This retrospective cohort study examined inpatient mortality and secondary outcomes of patients with myxedema coma from 2016 to 2020 using the NIS database. Patients were selected using International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM) codes and divided into weekday and weekend admission groups. From 174,776,205 discharges, 5095 patients were included. Mean age of admitted patients was higher on weekdays (67.1 year) than weekends (66.5), with females constituting 69.4% and 67.4% of admissions, respectively. Weekend admissions had higher odds of inpatient mortality compared to weekdays [adjusted odds ratio (aOR): 1.9, p = 0.01]. The overall mortality rate for myxedema coma rose from 6.8% in 2016 to 13.4% in 2020 (p-value = 0.01). No significant difference in the length of stay, hospitalization cost, and charges, blood transfusion, acute kidney injury requiring dialysis, acute respiratory failure requiring intubation and parenteral nutrition was noted between weekday and weekend admissions. Further studies are needed to identify factors contributing to this disparity and to confirm the findings of increasing mortality related to myxedema.

Keywords: Myxedema coma, Weekend admissions, Mortality rate, National inpatient sample

1. Introduction

Myxedema coma is a severe manifestation of hypothyroidism and is associated with a significant risk of death, making it a life-threatening emergency. It is estimated that the approximate incidence of myxedema coma is 0.22 cases per million population each year.[2,3] Previous research and recent studies indicate that the mortality rate for myxedema coma, even with prompt treatment, varies between 30 and 60%, with more recent findings reporting rates closer to 30%.[3–5]

The "weekend effect" refers to the observation that patients admitted to hospitals on weekends often experience worse outcomes compared to those admitted on weekdays. This phenomenon has been well-documented across various medical conditions, including stroke, myocardial infarction, and pulmonary embolism. The weekend effect is typically attributed to factors such as reduced staffing levels, limited availability of specialized care, and delays in diagnostic and therapeutic interventions during weekends. Despite extensive research on the weekend effect

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for these and other common acute conditions, there is a notable gap in the literature regarding its impact on patients with rare and life-threatening conditions such as myxedema coma.[6] Existing studies have primarily focused on more prevalent conditions, leaving the effects on myxedema coma underexplored.

The lack of large database studies in the past due to the rarity of myxedema coma has made it difficult to determine the outcomes and factors associated with mortality in this condition.[4,7–9] Addressing this gap is crucial, as understanding the weekend effect in the context of myxedema coma could lead to targeted interventions aimed at improving outcomes for this vulnerable patient population. Our study aims to address this gap by utilizing a large, nationwide database from the United States to examine the impact of weekend admissions on the outcomes of patients with myxedema coma. Specifically, we investigate how the day of admission affects inpatient outcomes such as mortality, morbidity, and resource utilization. This research provides valuable insights into potential disparities and can guide future healthcare policies and resource allocation.

2. Materials and methods

2.1. Study design and database description

This was a retrospective cohort study of adult patients hospitalized with the principal diagnosis of myxedema coma using data from the National Inpatient Sample (NIS) involving the period from 2016 to 2020 in the United States. The NIS, which is a component of the Healthcare Cost and Utilization Project (HCUP), is obtained from the State Inpatient Databases (SID) which covers 98% of the population in the United States of America. The Agency for Healthcare Research and Quality (ARQ) is responsible for maintaining the NIS, which is the largest publicly accessible, de-identified all-payer inpatient database in the United States. It is structured as a stratified probability sample to depict all non-federal acute care hospitals across the nation. Hospitals are categorized based on ownership/control, bed size, teaching status, urban or rural location, and geographic region. A 20% sample of hospitals is taken, and each hospital discharge was weighted to make the sample nationally representative. The weight is calculated by dividing the total number of discharges across all acute care hospitals in the United States by the number of discharges in the 20% sample.

2.2. Study patients

Patients hospitalized with a primary diagnosis of myxedema coma were selected using the International Classification of Disease, Tenth Revision with Clinical Modification (ICD-10-CM) code (E035), which has been in use in the United States since October 2015. Individuals under the age of 18 were excluded from the study. The patients were divided into two groups, weekday, and weekend, according to the day of admission (Fig. 1). The study was deemed exempt from Institutional Review Board approval due to the use of de-identified, publicly accessible data.

2.3. Study variables and outcomes

In this study admissions occurring between 12:00 AM Monday and 11:59 PM Friday were classified as weekday admissions, while those occurring between 12:00 AM Saturday and 11:59 PM Sunday were classified as weekend admissions. The primary outcome measure was in-hospital mortality, as provided by the NIS. In addition to the primary outcome, the study investigated several secondary outcomes such as the duration of hospitalization (length of stay), total hospitalization charges and costs, acute kidney injury (AKI) requiring dialysis, circulatory shock requiring vasopressors, acute respiratory failure (ARF) requiring intubation, palliative care consult and total parenteral nutrition (TPN). The outcomes were adjusted for several potential confounding variables, including the patient's age, gender, race, median income in the patient's zip code (grouped into four hierarchical categories), patient comorbidities as measured by the Charlson Comorbidity Index for administrative data, insurance status, hospital location, hospital teaching status (whether it was a teaching or non-teaching hospital), and hospital bed size.

2.4. Statistical analysis

The statistical analysis was conducted using Stata version 14 (StataCorp, College Station, TX). The NIS data, derived from a complex sampling design incorporating stratification, clustering, and weighting, required the application of appropriate survey weights provided by the NIS to ensure accurate national estimates.

To account for the stratified and clustered sampling design of the NIS, we utilized the 'svy' commands in Stata. This setup specified the primary sampling unit (HOSP_NIS), the discharge weight (DISCWT), and the strata (NIS_STRATUM),

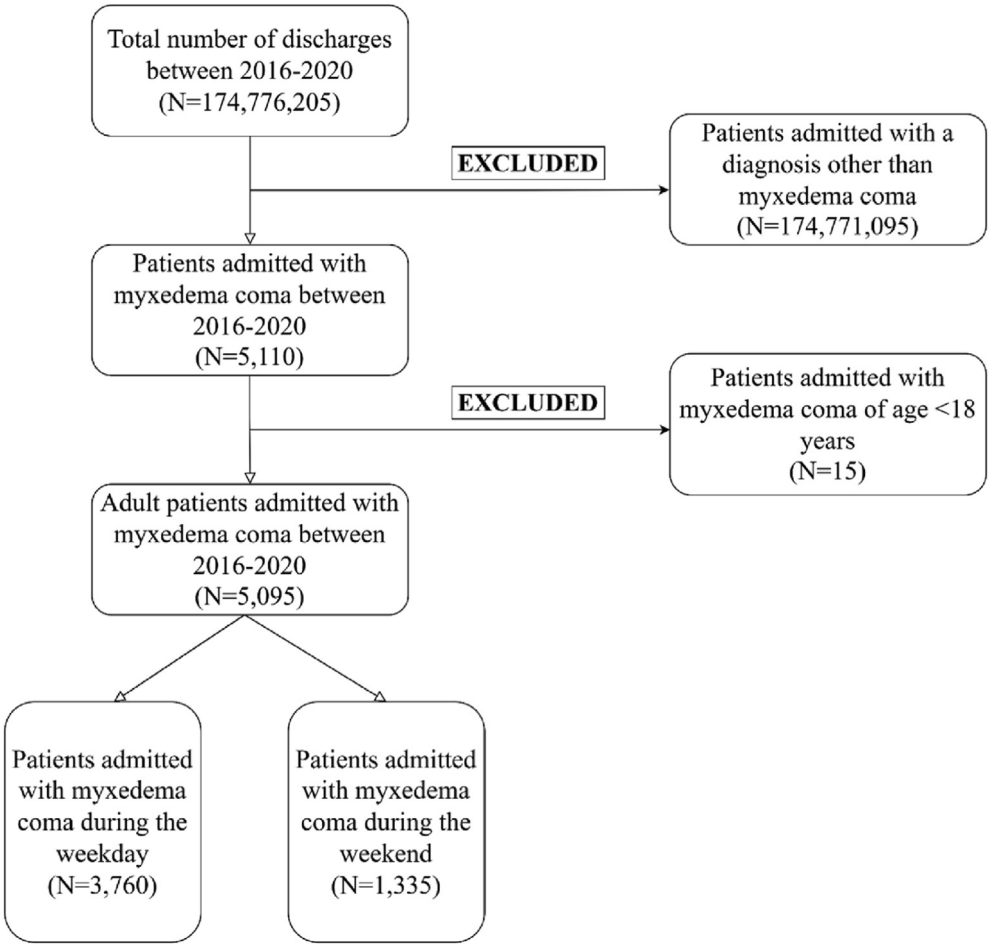


Fig. 1. Patient selection flow diagram.

ensuring that our estimates were representative of the national population. Confidence intervals were adjusted for the complex survey design using Taylor series linearization, a method implemented in Stata's survey procedures to ensure accurate estimation of standard errors and confidence intervals, accounting for the survey design effects. By employing these methods, we ensured that our analyses accurately reflected national estimates and were robust against the complex sampling design of the NIS.

Our statistical analysis did not follow the observed vs. expected method with an expected value of 5/7ths. Instead, we used standard statistical procedures to compare proportions and means between groups. Specifically, Fisher's exact test was used to compare proportions, while continuous variables were assessed using the Student t-test. Additionally, we conducted univariable logistic regression analysis to extract unadjusted odds for primary and secondary outcomes. We built a multivariable logistic regression model to adjust for confounders, incorporating all factors significantly associated with the outcome on univariable analyses with p-values <0.2.[10] Clinically important variables were included in the model based on literature, regardless of their significance in univariable analysis. This dual approach ensures that our models are robust and account for known confounders as well as those identified in our dataset.

This combined method helps to mitigate potential suppressor or interactive effects, which could obscure the true relationship between predictors and outcomes if only a single criterion were used. By including variables significant in the literature, we ensure that critical confounders are not omitted from our models, thereby enhancing the validity of our findings." Logistic regression was used for binary outcomes, and linear regression for continuous outcomes. In this study, statistical significance was determined by a 2-sided threshold of 0.05 for all p values.

3. Results

3.1. Patient characteristics

Of the 174,776,205 weighted discharges recorded in the NIS database between 2016 and 2020, 5095 patients satisfied the study's inclusion criteria. The patient and hospital characteristics of the two groups are detailed in Table 1. Within the study population, 26.2% (n = 1335) were admitted on weekends, while the remaining 73.8% (n = 3760) were admitted on weekdays. The mean age of patients admitted on weekdays was 67.2, compared to an average age of 66.5 years for those admitted on weekends.

We found that myxedema coma was more prevalent in white females, households belonging to the lowest income quartile and patients with Medicare insurance. Most of these patients were admitted to large and teaching hospitals. However, no significant differences in patient and hospital characteristics were observed between the weekend and weekday groups based on the statistical analysis (Table 1).

3.2. Primary outcome: inpatient mortality based on the day of admission

Patients with myxedema coma had an all-cause mortality rate of 11.6%. Patients admitted on the weekend had an all-cause mortality rate of 13.1%, higher than the rate observed for weekday admissions (8.4%). After statistically controlling for confounding variables through multivariate logistic regression analysis, patients with myxedema coma admitted on weekends had greater inpatient mortality compared to those admitted on weekdays [adjusted odds ratio (AOR): 1.9, 95% confidence interval (CI): 1.2–3.1, $p = 0.01$].

3.3. Secondary outcome: mortality trends

Overall mortality rate for patients with myxedema coma increased from 6.8 in 2016 to 13.36 in 2020

Table 1. Comparison of myxedema coma patients' characteristics by weekend and weekday admission.

	Weekday admissions (n = 3760)	Weekend admissions (n = 1335)	*p*-value
Female gender (%)	69.4%	67.4%	0.54
Age (mean)	67.1	66.5	0.34
Charlson co-morbidity index (%)			0.61
1	27.1%	27.2%	
2	21.0%	18.0%	
3	51.9%	54.8%	
Median household income (quartile) (%)			0.34
1	31.0%	33.3%	
2	29.5%	24.0%	
3	24.3%	24.4%	
4	15.2%	18.2%	
Hospital region (%)			0.54
Northeast	16.8%	15.0%	
Midwest	22.2%	25.5%	
South	39.4%	36.0%	
West	21.7%	23.6%	
Hospital bed size (%)			0.38
Small	20.1%	17.6%	
Medium	31.3%	28.8%	
Large	48.7%	53.6%	
Hospital teaching status (%)			0.61
Non-teaching	28.6%	27.0%	
Teaching	71.4%	73.0%	
Race (%)			0.68
White	69.2%	69.3%	
Black	16.4%	14.0%	
Hispanics	8.6%	9.3%	
Others	5.9%	7.4%	
Insurance status (%)			0.83
Medicare	65.1%	67.5%	
Medicaid	18.3%	18.4%	
Private	10.3%	8.6%	
Uninsured	6.2%	5.5%	

($p = 0.01$). Similar increase in mortality pattern for weekday admissions was observed with highest inpatient mortality rate 11.9%, in 2020 (p-value 0.03). Weekend mortality rates, however, showed no significant change over time (12.7% in 2016 to 15.4% in 2020, $p = 0.35$). These trends are depicted in Fig. 2.

3.4. Hospital length of stay

The overall mean LOS for the study population was 9.4 days, with patients admitted on weekdays experiencing a shorter mean LOS of 9.1 days compared to those admitted on weekends, who had a mean LOS of 10.3 days. After accounting for confounding factors using multivariate linear regression, there was no significant difference in adjusted mean difference for length of stay (−0.2 days) between the weekend and weekday admission groups in our sample population ($p = 0.844$).

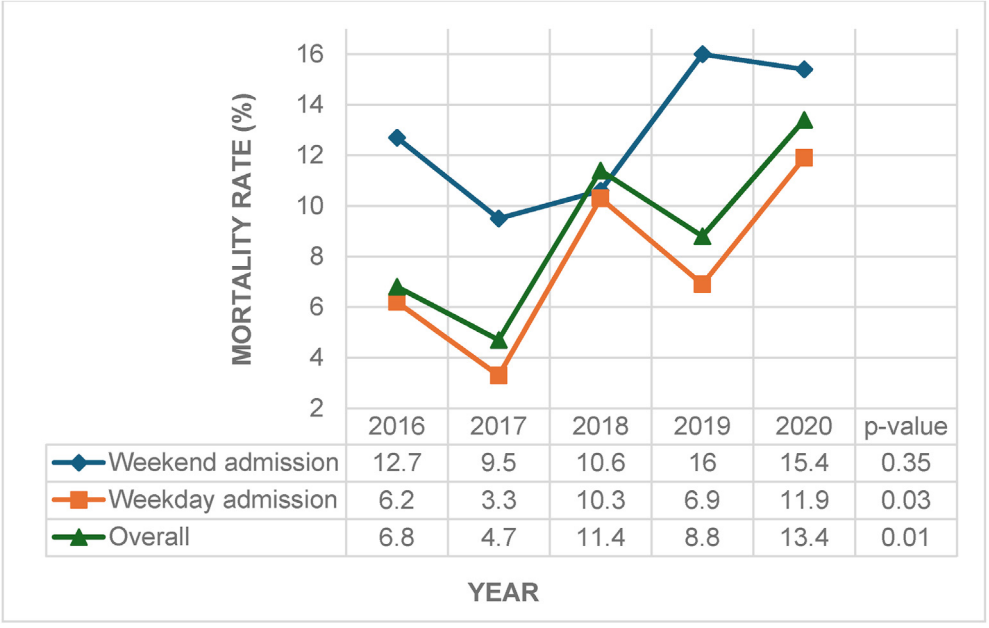
3.5. Resource utilization

Total hospitalization cost and charges in U.S. dollars (USD), blood transfusions, and parenteral nutrition were markers used to measure resource utilization. The mean hospitalization charges were $89,423 (95% CI: 82,291–96,556), and $112,594 (95% CI: 90,869–134,319) for patients admitted on weekdays and weekends, respectively. However, after adjusting for the confounding variables outlined in the study variables and outcomes, no significant difference was observed in the total hospitalization charges between the two groups (the adjusted mean difference in hospital charge for weekend admission was $16,354 (95% CI: −6102 to 38,810; $p = 0.153$).

The mean hospital cost showed a similar pattern; weekend admissions had a higher mean cost of $26,892 (95% CI: 21,851–31,934) than weekday admissions at $22,402 (95% CI: 20,622–24,183). Nonetheless, there was no statistically significant difference between the two groups after adjusting for confounding variables using multivariate linear regression analysis. Moreover, there was no significant difference in the requirement for TPN between the two groups (AOR 0.8, 95% CI: 0.3–1.9, $p = 0.57$).

3.6. Morbidity

Although the rate of AKI requiring dialysis was higher for weekend (2.3%) than for weekday admissions (1.2%), no statistically significant difference was found between the two groups after accounting for confounding factors. Similar trends were also seen in ARF requiring intubation which was higher on weekend admissions (35.6%) compared to weekday admissions (29.5%). After adjusting for multiple hospital and patient level variables, no significant difference was noted between groups. There was no significant variation in the occurrence of circulatory shock requiring vasopressors between weekday and weekend admissions, consistent with the observed patterns in morbidity (aOR = 1.8; $p = 0.081$).



	2016	2017	2018	2019	2020	p-value
Weekend admission	12.7	9.5	10.6	16	15.4	0.35
Weekday admission	6.2	3.3	10.3	6.9	11.9	0.03
Overall	6.8	4.7	11.4	8.8	13.4	0.01

Fig. 2. Inpatient mortality for myxedema coma over time.

Table 2. Observed rates and adjusted odds ratios (AOR) for primary and secondary outcomes in myxedema coma.

Outcomes	Weekday admissions (95% CI)	Weekend admissions (95% CI)	Adjusted odds ratio (AOR) (95% CI)	*p*-value
Mortality, %	8.4 (6.6–10.6)	13.1 (9.6–17.7)	1.9 (1.2–3.1)	0.01
Length of stay, mean, days	9.1 (8.4–9.7)	10.3 (8.2–12.4)	−0.2[e] (−1.9, 1.6)	0.84
Total hospital charges, mean, USD	89,423 (82,291–96,556)	112,594 (90,869–134,319)	95,512[f] (87,753–103,272)	0.15
Total hospital cost, mean, USD[a]	22,403 (20,622–24,183)	26,892 (21,851–31,934)	2,221[f] (−3188, 7630)	0.42
ARF[b] requiring intubation, %	29.5 (26.36–32.89)	35.6 (30.12–41.45)	1.4 (0.98–1.86)	0.06
Circulatory shock requiring vasopressors, %	3.9 (0.1–6.1)	6.7 (4.3–10.4)	1.8 (0.8–2.4)	0.08
AKI[c] requiring dialysis, %	1.9 (1.1–3.1)	2.3 (1.0–4.9)	0.8 (0.2–2.5)	0.66
Palliative care, %	12.1 (10.0–14.6)	12.4 (8.9–16.9)	1.1 (0.7–1.8)	0.59
TPN,[d] %	3.7 (2.6–5.4)	3.4 (1.8–6.4)	0.8 (0.3–1.9)	0.57

In the multivariate regression analysis, the data has been adjusted for the following variables: age, gender, race category, charlson comorbidity index, ZIP code income quartile, hospital region, hospital bed size, teaching hospital status, insurance type, coronary artery disease, hypertension, hyperlipidemia, congestive heart failure, chronic kidney disease, obesity, and diabetes mellitus.

[a] United States Dollar.
[b] Acute respiratory failure.
[c] Acute kidney injury.
[d] Total parenteral nutrition.
[e] Adjusted mean difference in days.
[f] Adjusted mean difference in USD.

3.7. Palliative care utilization

Weekend admissions showed a marginal increase in palliative care utilization (12.4%) compared to weekday admissions (12.1%). After adjusting for confounders, no significant difference was observed between groups (aOR = 1.1; 95% CI 0.7–1.8) (Table 2).

4. Discussion

Myxedema coma is characterized by a decline in cognitive function and hypothermia. It may also manifest as hypotension, bradycardia, hyponatremia, hypoglycemia, and hypoventilation. Treatment should not be postponed while awaiting blood test results and should instead be initiated immediately based on clinical suspicion.[7] The management of myxedema coma involves a multi-disciplinary approach that requires admission to the intensive care unit (ICU). Thyroid supplementation is the mainstay of treatment; however, there is some controversy surrounding it due to the lack of clinical trials comparing various methods. The preference for administration of T3, T4, or both varies among experts.[8,11]

Our analysis of the NIS data from 2016 to 2020 indicated that weekend admissions for myxedema coma were associated with higher mortality rates when compared to weekday admissions. However, weekend admissions were not associated with significant differences in hospital LOS, resource utilization, AKI requiring dialysis, ARF requiring intubation, circulatory shock requiring vasopressors, use of TPN and palliative care use. Although overall and weekday mortality rates increased from 2016, there was no significant difference in the mortality trend for weekend admissions.

Patients hospitalized with myxedema coma had a mortality rate of 11.6%. However, another retrospective study utilizing the national inpatient database from Japan between July 2010 and March 2013 showed a considerably higher inpatient mortality rate for myxedema coma, 29.5%. Mean age in the Japanese study was 77 years, surpassing that of the U.S. data, which may explain the increased mortality rate. Nevertheless, the sex distribution of this study and Ono et al., were similar.[5] A previous study conducted from 1999 to 2006 at a single center in South Asia, involving 23 patients, reported a mortality rate of 53%. The higher mortality rate may be associated with resource scarcity and limited access to diagnostic and treatment facilities in developing countries.

Our study revealed a 91% increase in the odds of mortality for weekend admissions compared to admissions done during the weekday. These findings are consistent with those of other studies investigating the effects of weekend admissions on various other medical conditions like stroke, acute myocardial infarction, and pulmonary embolism.[12–14] Our findings add to the existing literature by demonstrating that the weekend effect is not only limited to more common conditions but also extends to rare and life-threatening conditions such as myxedema coma. These findings underscore the importance of further research to identify and mitigate factors contributing to the weekend effect, thereby

improving patient outcomes across all days of the week.

We identified several factors from our literature review that may contribute to the increased mortality observed during weekend admissions. These include reduced staffing levels and limited resources.[15] The quality of care may also vary depending on the day of the week; different providers may have different levels of expertise. Additionally, delays in seeking medical attention on weekends or differences in the severity of the disease among patients admitted on weekends may also contribute to elevated mortality rates.[16] By understanding and addressing these systemic issues, healthcare systems can develop strategies to ensure consistent and high-quality care regardless of the day of admission.

Myxedema coma exhibited increasing mortality from 2016 to 2020. This increase in mortality trends is concerning; due to the rarity of the condition, there are insufficient large-scale studies available to compare mortality trends over time. In 2020, myxedema coma mortality spiked at 13.4%, coinciding with the COVID-19 pandemic and possibly concurrent with COVID-19 infection. However, evaluating this impact was outside the scope of this study. Nevertheless, many studies have demonstrated an increase in mortality for non-COVID-19 related hospitalizations which occurred during the pandemic.[17,18] According to a recent study that examined the total number of admissions from the COVID-19 research database from January 2019 to December 2020, odds of in-hospital death among non-COVID-19 patients during the pandemic were 1.2 times higher than before the pandemic.[17,19] This increased risk of death may be attributed to disruptions in healthcare continuity, inpatient services, and resource availability resulting from the pandemic.

Our research is subject to limitations. Retrospective studies utilizing administrative and claims-based datasets can be prone to misclassification, missing codes, and inaccurate coding. These factors may impact precision and reliability of our results. However, we utilized multivariate logistic regression models to account for multiple patient and hospital-level characteristics, including co-morbidities, to adjust for any potential confounders. Despite adjustments, a chance of residual confounding remains, although the likelihood is low.

The severity of myxedema coma was not addressed; HCUP data does not include information on laboratory values. Nevertheless, we utilized the Charlson comorbidity index, a well-established and validated prognostic tool, to adjust for comorbidity burden. All-cause inpatient mortality rate for patients admitted with a primary diagnosis of myxedema coma was analyzed; NIS does not contain enough data to determine the exact cause of death. In our opinion, additional studies are essential to address the limitations encountered in this study.

Despite limitations outlined earlier, the study has several strengths. It is the first nationwide investigation examining the impact of day of admission on hospitalization outcomes for patients with myxedema coma The use of the NIS database, a multicenter and nationally representative dataset, enhances the study's statistical power by providing a large sample size. This larger sample size reduces the probability of a type II error (beta error) compared to single-center studies. The NIS, being the largest publicly available all-payer inpatient database, includes data on the inpatient population at a national level, which further strengthens the robustness and reliability of the analysis.[20] Also, the characteristic variables found in the NIS database provided an opportunity to investigate variables that are not usually available in single-center studies, such as household income estimates, hospitalization costs, and hospital-related factors. NIS eliminates bias associated with practice patterns arising in single or multi-center studies.

5. Conclusion

Patients with myxedema coma admitted on weekends had higher inpatient mortality compared to those admitted on weekdays after adjustment for confounders. The overall all-cause mortality rate for patients with myxedema coma has been increasing, from 6.8 in 2016 to 13.4 in 2020, with the highest mortality observed in 2020. There was no significant difference in adjusted mean difference for the length of stay, resource utilization, and morbidity outcomes between weekday and weekend admission groups. Further studies are necessary to investigate factors contributing to the increased mortality in patients with myxedema coma admitted on weekends and to assess the effectiveness of interventions aimed at reducing the disparity in mortality rates by day of the week.

Disclaimer

This manuscript has not been presented at any conference or meeting, nor has it been submitted to any other publication for consideration. It is currently available as a pre-print with the DOI: https://doi.org/10.21203/rs.3.rs-3085786/v1.

Ethics information

The protocol for this study was submitted to the Institutional Review however was exempted from review as this study was based on de-identified publicly available data.

Funding information

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Data availability

The data analyzed in the study is publicly available through Healthcare Cost and Utilization Project (HCUP).

Conflicts of interest

There are no financial conflicts of interest to disclose.

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