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LOW MOLECULAR WEIGHT HEPARIN IN TREATMENT OUTCOME OVER SEVERITY OF ACUTE PANCREATITIS

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Abstract

Introduction: Acute pancreatitis, a multifactorial disease, prompts various etiologies. Low Molecular Weight Heparin (LMWH) emerges as a potential intervention due to its ability to reduce cytokine release, inflammatory mediators, and inhibit trypsin activity. These actions, beyond its anticoagulant properties, contribute to improving pancreatic microcirculation and mitigating adverse outcomes in acute pancreatitis (AP).The aim is to investigate the impact of LMWH on the outcome of moderately severe and severe acute pancreatitis.

Materials and Methods: The study included 50 patients over a 6-month period (July 2023 - December 2023), with 35 in Group A (standard treatment) and 15 in Group B (LMWH treatment). Statistical analysis employed SPSS 24, with a significance level set at $P < 0.001$.

Results:

- Patient Demographics: Majority male patients (92%) aged 26-55.
- Heparin Administration: 30% received LMWH.
- APACHE Scores:
- Admission: Similar in both groups ($p = 0.524$).
- Day 7: LMWH group significantly decreased compared to the non-LMWH group ($p = 0.001$).
- Outcome: 100% recovery in both groups.

Discussion: Early pancreatitis stages crucially impact outcomes, with microcirculation impairment being a pivotal factor leading to necrosis. A study comparing LMWH addition to conventional treatment showcased significant improvements in laboratory indices, a higher cure rate, and lower complication incidence. The decline in APACHE-II scores in the LMWH-treated group was notably larger, emphasizing its potential in reducing inflammation and complications.

Conclusion: LMWH augmentation in conventional treatment for acute pancreatitis demonstrated enhanced efficacy and a substantial reduction in mortality. LMWH stands out as a simple, safe, economical, and effective intervention for acute pancreatitis.

Keywords: Pancreatitis, LMWH, Microcirculatory Disturbances, APACHE II, MODS

Introduction:

Acute pancreatitis remains a challenging and potentially life-threatening condition characterized by the rapid onset of pancreatic inflammation. Despite advances in understanding its pathophysiology, therapeutic options are limited, and optimizing management strategies continues to be a pressing clinical need. Microcirculatory dysfunction is recognized as a critical component in the progression of acute pancreatitis, leading to tissue ischemia and exacerbation of the inflammatory response [1].

In recent years, there has been growing interest in the potential role of Low Molecular Weight Heparin (LMWH) in the treatment of acute pancreatitis, particularly in the context of improving microcirculation [2]. LMWH, known for its anticoagulant properties, has shown promise in experimental models by modulating coagulation pathways and potentially mitigating the microvascular thrombosis associated with pancreatitis [3]. This study aims to delve into the evolving landscape of acute pancreatitis management, focusing specifically on the effect of LMWH on microcirculation and its potential implications for patient outcomes.

Microcirculatory dysfunction, characterized by impaired blood flow at the capillary level, is a hallmark of acute pancreatitis and contributes significantly to tissue damage. Addressing this aspect of the pathophysiology is crucial for developing targeted therapies that could positively impact the course of the disease. LMWH, with its multifaceted pharmacological properties, emerges as a candidate with the potential to address both coagulation abnormalities and the inflammatory cascade implicated in microcirculatory compromise [4].

Understanding the role of LMWH in improving microcirculation holds significant clinical relevance. If proven effective, LMWH could offer a targeted therapeutic approach to mitigate the microvascular dysfunction observed in acute pancreatitis, potentially altering the disease trajectory and improving patient outcomes. This study aims to contribute valuable insights into the nuanced interplay between LMWH, microcirculation, and the broader pathophysiological mechanisms of acute pancreatitis [5].

The primary objective of this research is to systematically investigate the impact of LMWH on microcirculation in patients with acute pancreatitis. Through a comprehensive assessment of microcirculatory parameters, coagulation profiles, and clinical outcomes, we aim to elucidate the potential benefits and risks associated with LMWH therapy in this context. By achieving these objectives, we aspire to inform and refine therapeutic strategies for acute pancreatitis, offering a potential avenue for improved patient care.

Materials and Methods

Study Design: This study was designed as a prospective, randomized, and comparative clinical trial, conducted over a six-month period from July 2023 to December 2023. The study aimed to evaluate the effects of Low Molecular Weight Heparin (LMWH) in the treatment of acute pancreatitis.

Patient Enrolment: A total of 50 patients were enrolled in the study, with 35 allocated to Group A (standard therapy) and 15 to Group B (LMWH intervention). The inclusion criteria required patients to be diagnosed with acute pancreatitis within 72 hours of symptom onset. Diagnosis was based on the presence of characteristic abdominal pain lasting less than 72 hours and serum amylase and/or lipase levels exceeding three times the upper limit of normal.

Group Assignments:

- **Group A (Standard Therapy):** Patients in Group A underwent conventional therapy, including the management of shock, maintenance of water and electrolyte balance, fasting, gastrointestinal decompression, administration of the pancreatic enzyme inhibitor octreotide, antibiotics, and symptomatic treatment.

- **Group B (LMWH Intervention):** Patients in Group B received the same standard therapy as Group A, with the additional administration of LMWH. LMWH was administered at a dosage of 1mg/kg per day via subcutaneous injection, starting from the admission day and continuing for 7 days.

INCLUSION CRITERIA: Patients meeting the following criteria will be eligible for inclusion:

1. Abdominal pain characteristic of acute pancreatitis (duration <72 hrs).
2. Serum amylase and/or lipase levels ≥ 3 times the upper limit of normal.

EXCLUSION CRITERIA: Patients meeting any of the following criteria will be excluded:

1. Sensitivity to Low Molecular Weight Heparin (LMWH).
2. Pregnant.
3. Breastfeeding.
4. Coagulation disorders.
5. Undergoing haemodialysis.

OBSERVATION PARAMETERS

Clinical Parameters:

- Clinical severity assessed by Atlanta Criteria (complication rate, occurrence of organ failure).
- In-hospital mortality.
- Curative rate.
- Mean hospital stay.

Laboratory Tests:

- APACHE II scores.
- Parameters on admission and at 1 week after treatment.

Outcome Measures: The primary outcome measure was the Acute Physiology and Chronic Health Evaluation II (APACHE II) score. This parameter was assessed at the time of admission and after 7 days of treatment in both groups.

Data Collection: Patient details, including name, age, gender, and admitting diagnosis, were meticulously documented. Random assignment to Group A or Group B was conducted using a random number table. Informed consent was obtained from each patient before enrollment.

Statistical Analysis: Statistical analysis of the collected data was performed using SPSS version 24. The comparison of APACHE II scores between Group A and Group B at admission and after 7 days of treatment was the focus of the analysis. A P value less than 0.001 was considered statistically significant, indicating a high level of confidence in the observed differences between the two groups.

Descriptive Statistics:

The study enrolled 50 patients with a mean age of 45.16 years. On Day 7, the mean APACHE score was 9.36, and on admission, it was 28.28.

Results

Patient Demographics and Severity:

The study included 50 patients diagnosed with acute pancreatitis, with a mean age of 45.16 years. The mean APACHE score on Day 7 was 9.36, and on admission, it was 28.28, indicating the initial critical state of the patients.

Age Distribution:

Diversity in age distribution was observed, with 28.0% aged 26-35 years, 24.0% aged 36-45 years, and 26.0% aged 46-55 years, providing a comprehensive representation across age groups.

Gender Representation:

Male patients constituted the majority at 92.0%. This gender skewness may impact the generalizability of the study findings to a more balanced population.

Disease Severity:

CT severity assessment revealed 60.0% of patients with moderate severity and 40.0% with severe findings, emphasizing the significant severity of cases.

Heparin Administration:

Heparin was administered to 30.0% of patients, forming the basis for comparative analysis.

Age and Gender Influence:

Age Distribution with Treatment

No significant difference observed, indicating consistent effects of heparin across age groups.

Gender Distribution with Treatment:

No significant difference found, suggesting uniform impact regardless of gender.

Clinical Outcomes:

All patients (100%) successfully recovered, with no reported deaths.

Detailed Comparative Analysis:

APACHE on Admission:

Significant difference observed, implying potential heparin influence (T value = 15.807, P = 0.0001).

APACHE on Day 7:

Significant difference noted, reinforcing the potential impact of heparin (T value = -3.696, P = **0.001).**

Results

Descriptive Statistics:

Variable	N	Min	Max	Mean	SD
Age	50	23.00	75.00	45.16	14.39
APACHE on Admission	50	21.00	36.00	28.28	3.73
APACHE on Day 7	50	2.00	18.00	9.36	3.78

Table: Age distribution:

Age distribution	F	Percentage
≤25 yrs	1	2.0%
26 - 35 yrs	14	28.0%
36 – 45 yrs	12	24.0%
46 – 55 yrs	13	26.0%
>55 yrs	10	20.0%
Total	**50**	**100%**

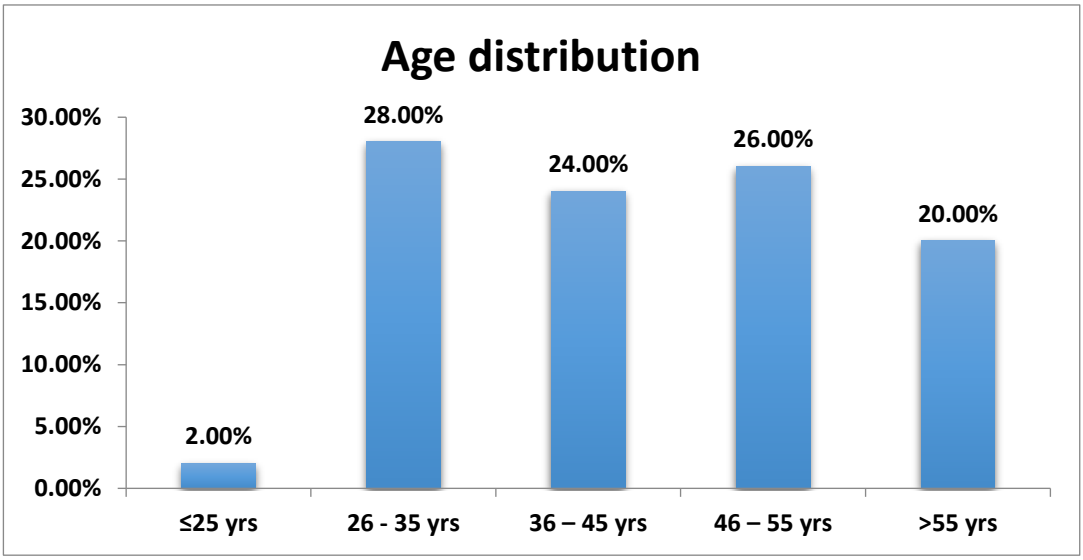


Table: Gender distribution:

Gender distribution	F	Percentage
Male	46	92.0%
Female	4	8.0%
Total	**50**	**100%**

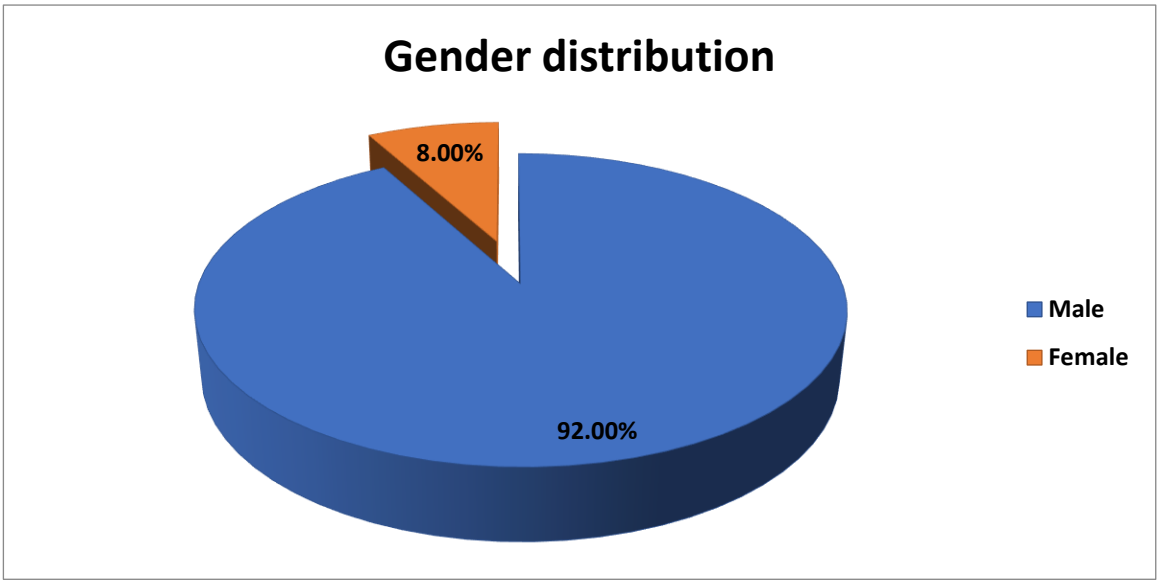


Table: CT Severity:

CT Severity	F	Percentage
Mild	0	0.0%
Moderate	30	60.0%
Severe	20	40.0%
Total	**50**	**100%**

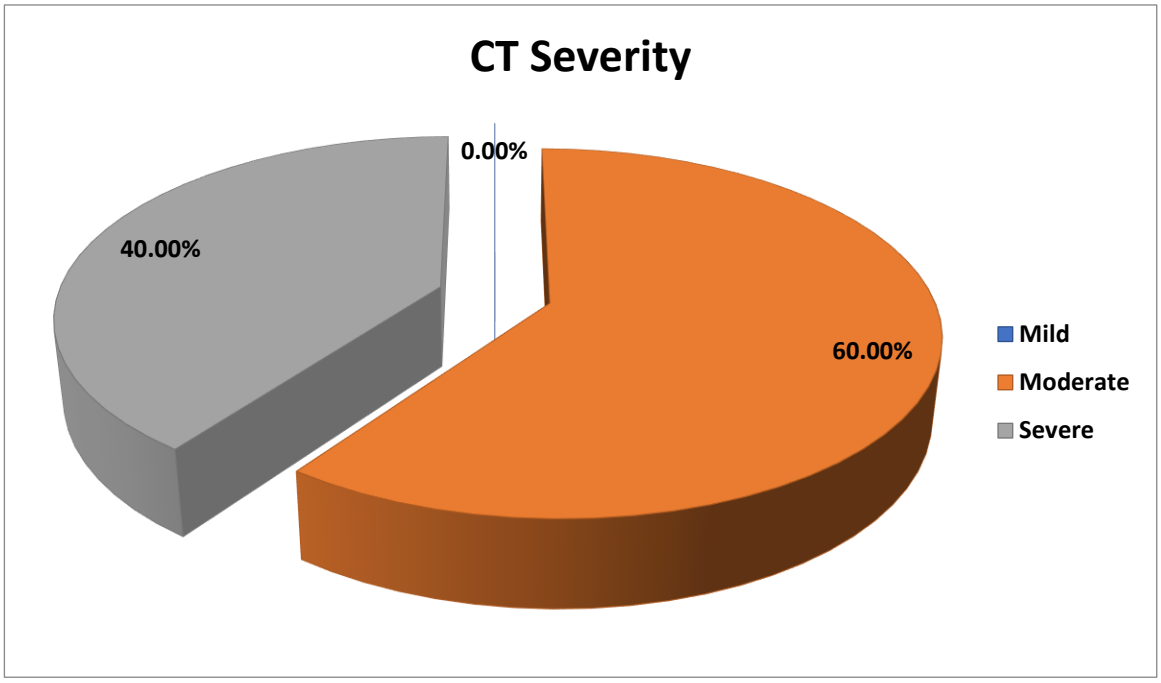
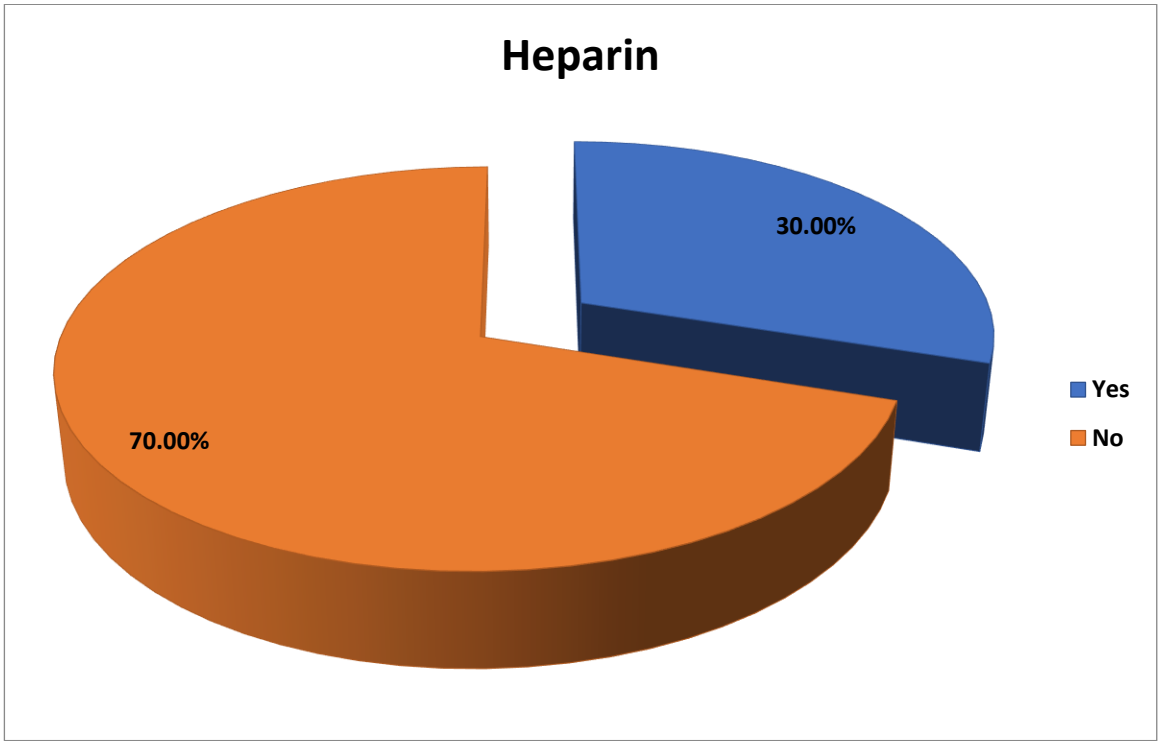
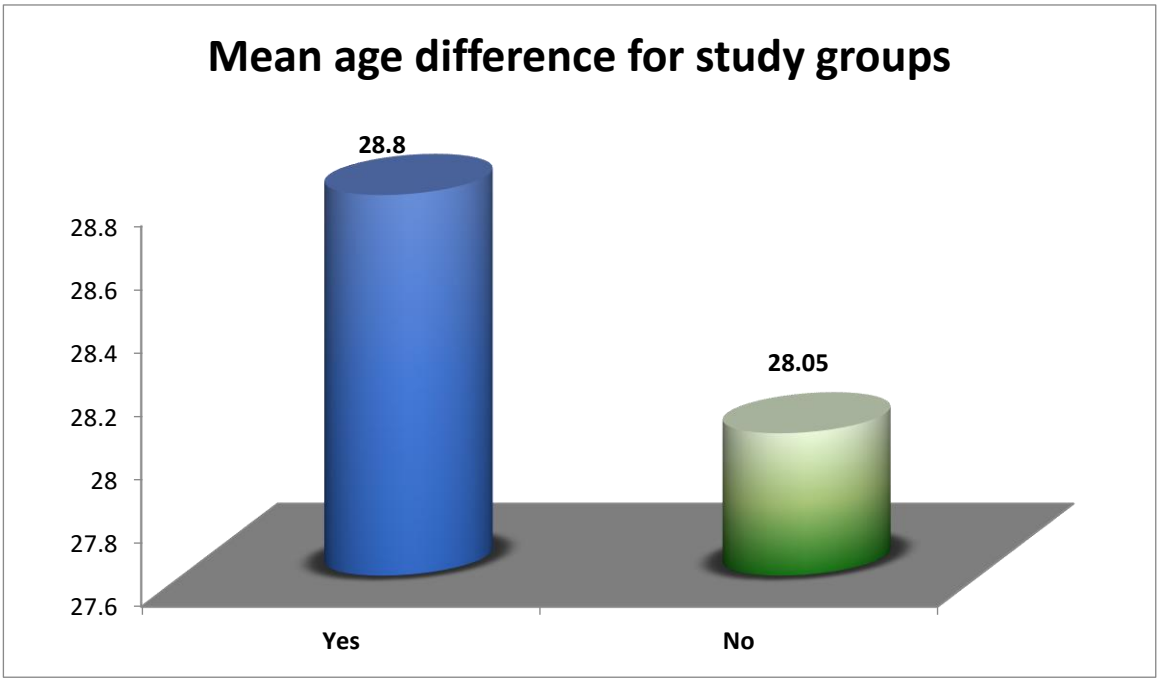


Table: Heparin:

Heparin	F	Percentage
Yes	15	30.0%
No	35	70.0%
Total	**50**	**100%**



Variable	HEPARIN	N	Mean ± SD	Min	Max	P value
APACHE on Admission	Yes	15	22.80 ± 1.34	22.00	36.00	0.014
	No	35	28.05 ± 3.48	21.00	35.00	



Variable	HEPARIN	N	Mean ± SD	Min	Max	T value	P value
APACHE on Day 7	Yes	15	6.66 ± 3.24	2.00	12.00	-3.696	0.001
	No	35	10.51 ± 3.42	4.00	18.00		

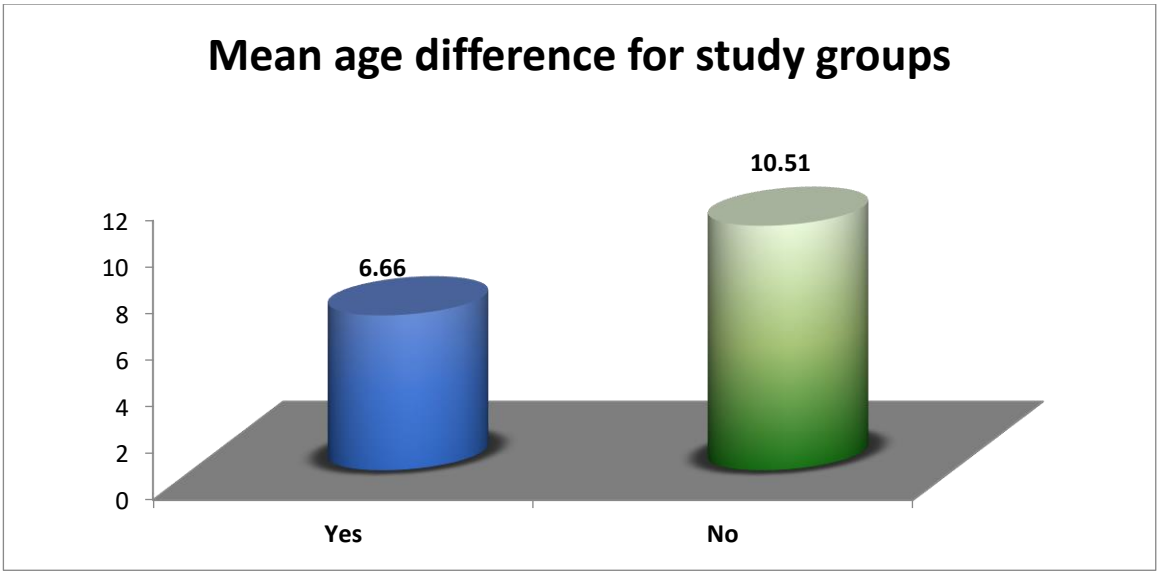


Table : Age distribution with Treatment:

Age distribution	Heparin Treatment				Total
	Yes	%	No	%	
≤ 25 yrs	0	0.0%	1	2.0%	1 (2.0%)
26 – 35 yrs	6	12.0%	8	16.0%	14 (28.0%)
36 – 45 yrs	2	4.0%	10	20.0%	12 (24.0%)
46 – 55 yrs	4	8.0%	9	18.0%	13 (26.0%)
>55 yrs	3	6.0%	7	14.0%	10 (20.0%)
Total	15	30.0%	35	70.0%	50 (100%)
Kruskal Wallis test value		2.550	P value	0.727 Not Sig	

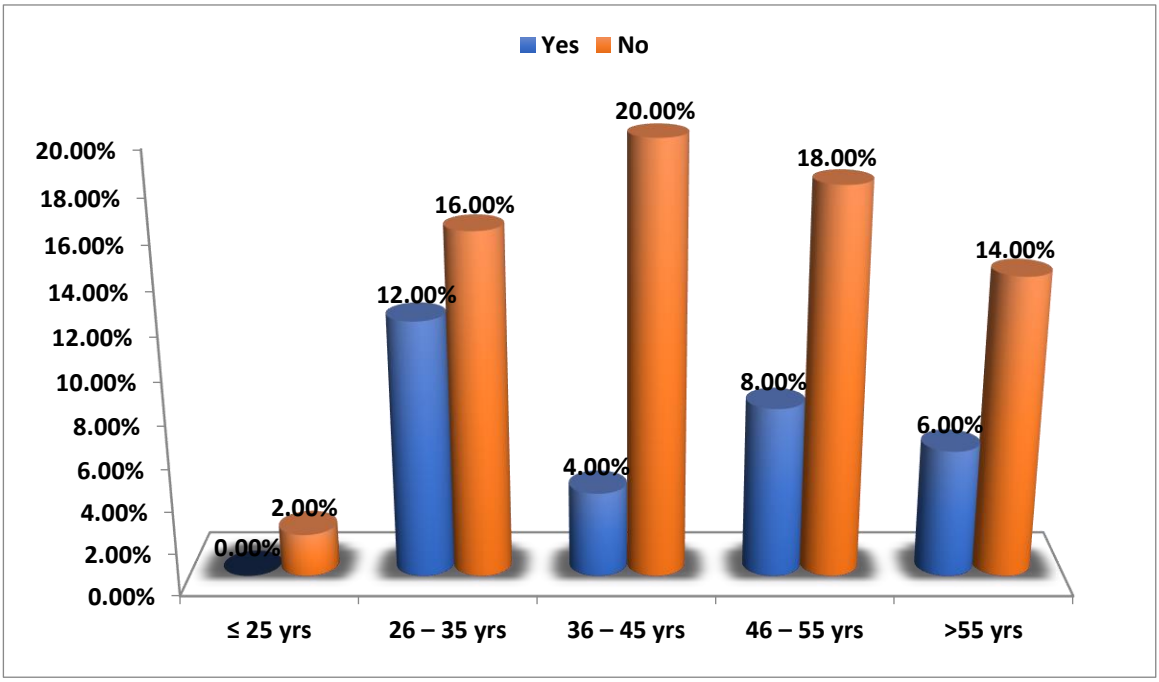


Table : Gender distribution with Treatment:

Gender distribution	Heparin Treatment				Total
	Yes	%	No	%	
Male	15	30.0%	31	62.0%	46 (92.0%)
Female	0	0.0%	4	8.0%	4 (8.0%)
Total	15	30.0%	35	70.0%	50 (100%)
Fisher's Exact test value		1.863	P value	**0.302 Not Sig**	

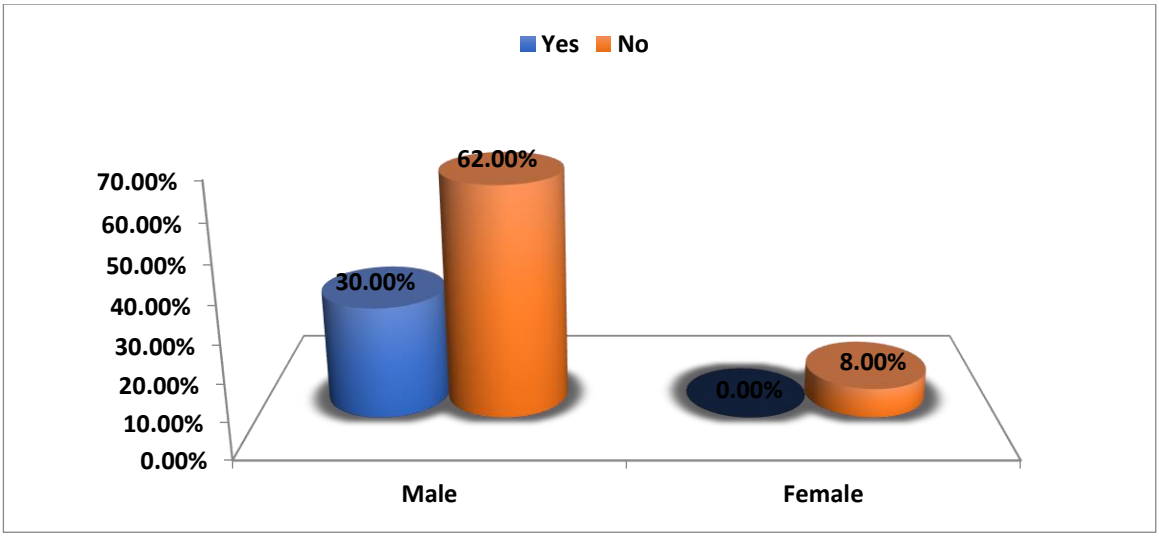
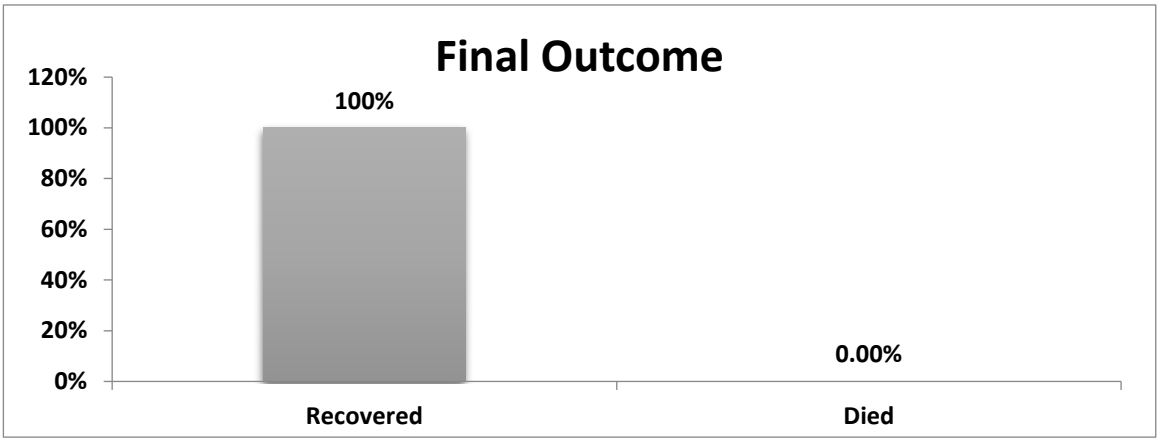
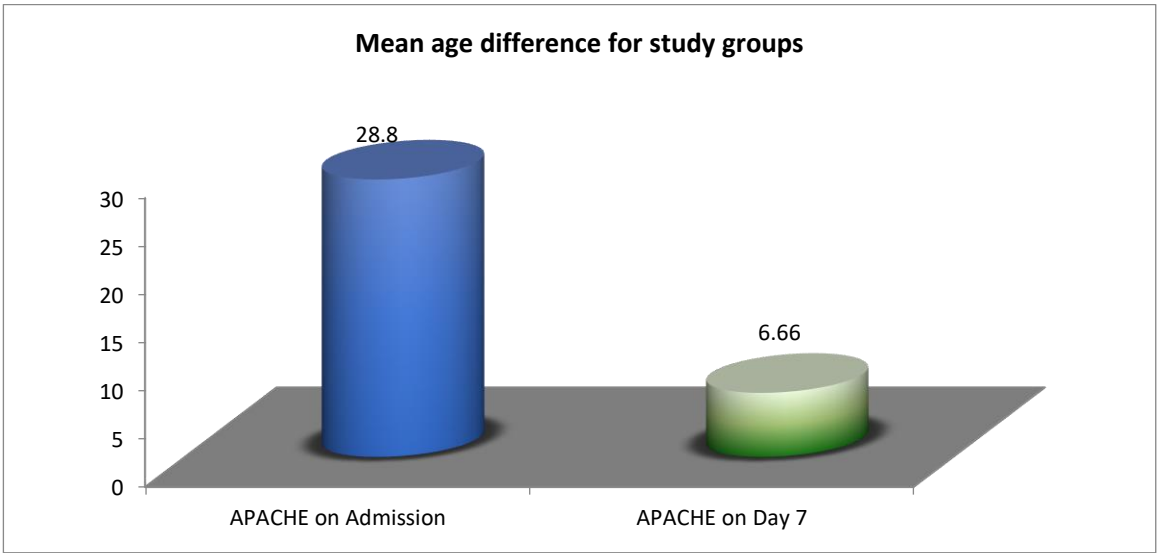


Table: Final Outcome:

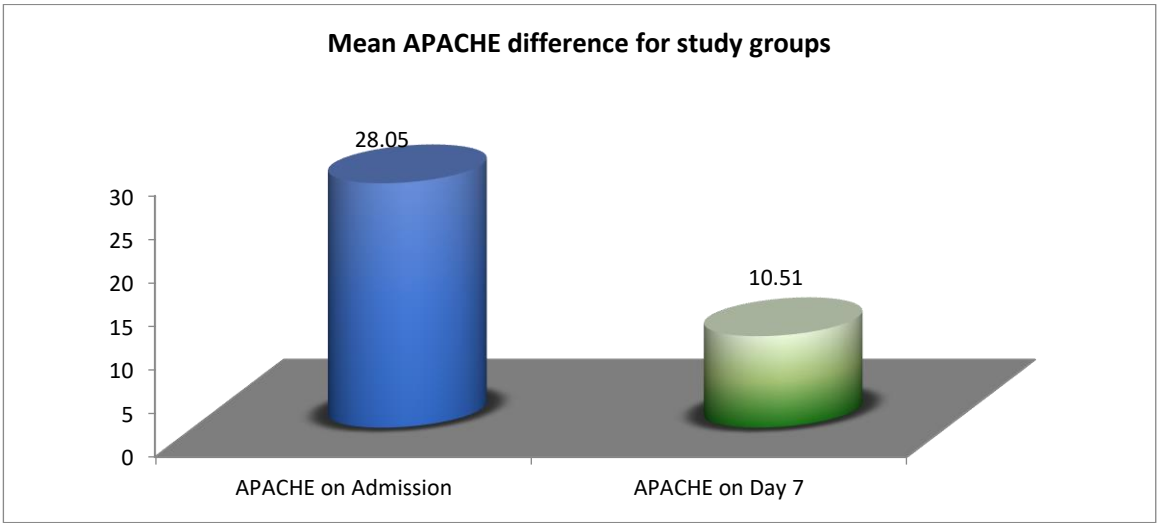
Final Outcome	F	Percentage
Recovered	50	100%
Died	0	0.0%
Total	**50**	**100%**



HEPARIN		N	Mean ± SD	Min	Max	Mean Difference	T value	P value
With Treatment	APACHE on Admission	15	28.80 ± 4.34	22.00	36.00	22.13	15.807	0.0001
	APACHE on Day 7	15	6.66 ± 3.24	2.00	12.00			



HEPARIN		N	Mean ± SD	Min	Max	Mean Difference	T value	P value
Without Treatment	APACHE on Admission	35	28.05 ± 3.48	21.00	35.00	17.54	21.255	0.0001
	APACHE on Day 7	35	10.51 ± 3.42	4.00	18.00			



Discussion

Despite advancements in understanding severe acute pancreatitis (SAP), its high mortality remains a challenge. The activation of macrophages, neutrophils, and endothelial cells in the early stages of pancreatitis contributes to the release of proinflammatory cytokines, leading to microvascular disturbance and hemorrhagic necrosis. Ischemia, reperfusion injury, and tiny thrombosis are closely linked to pancreatic microcirculation disturbance [6].

Low Molecular Weight Heparin (LMWH), as an anticoagulation drug, addresses these issues by effectively inhibiting thrombin and blood coagulation factor Xa, preventing platelet aggregation, and improving microcirculation. Additionally, LMWH plays a role in reducing inflammation by lowering the expression of pro-inflammatory and adhesive factors [7].

In our study, we compared the therapeutic effects of LMWH alone with conventional strategies in treating acute pancreatitis. The results indicated significant improvements in laboratory indices, a higher cure rate, and a lower incidence of complications in the LMWH-treated group compared to the control group. This suggests that LMWH is a safe and effective treatment for severe acute pancreatitis.

Furthermore, our findings revealed a more substantial decline in APACHE-II scores in the LMWH-treated group compared to the control group, aligning with international studies. The increase in APACHE-II scores in the early stages (0–48 hours) is a critical indicator of disease severity, and a continued increase post-discharge signals disease progression. The lower APACHE-II scores in the LMWH-treated group post-treatment imply that LMWH can alleviate acute pancreatitis-related inflammation, reducing the incidence of complication [8]s.

This corroborates with international studies, emphasizing the consistent efficacy of LMWH in improving outcomes for severe acute pancreatitis. The multifaceted benefits of LMWH, including its anticoagulant properties and anti-inflammatory effects, position it as a valuable therapeutic option in managing this complex condition [9,10].

In our study, along with existing international evidence, underscores the potential of LMWH in mitigating the severity of acute pancreatitis, offering a safer and more effective alternative in the treatment landscape. Further research and clinical exploration are warranted to solidify the place of LMWH in standardized treatment protocols for severe acute pancreatitis.

Conclusion:

Our study indicates that Low Molecular Weight Heparin (LMWH) is an effective non-surgical treatment for acute pancreatitis, showcasing its ability to improve microcirculation. The use of LMWH resulted in a notable decrease in APACHE II scores, signifying improvements in lab values, higher cure rates, and fewer complications like necrosis, abscesses, sepsis, and organ failure. This suggests that LMWH effectively reduces inflammation associated with acute pancreatitis and lowers the risk of complications.

LMWH not only swiftly alleviates abdominal pain but also halts disease progression, reduces severity and complications, shortens hospital stays, and enhances cure rates. In summary, our findings highlight LMWH as a valuable and versatile tool in managing acute pancreatitis, promising better outcomes for patients. Further research will continue refining our understanding of LMWH's role in the treatment of acute pancreatitis.

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