RESEARCH PAPER

Dosage Optimization of enoxaparin in the treatment of cardiovascular diseases in Egyptian obese patients

Abdel-Hameed Ibrahim Mohamed Ebid[1]; Ahmed Gaafar[2]; Hadeer Mohamed Gamal Mohamed Fahmi Ali Saleh[3]; Sara M.M. Abdel-Motalebm[4]

[1]Professor of Clinical Pharmacy and Head of Pharmacy Practice Department, Faculty of Pharmacy, Capital University, Egypt

[2]Associate Professor of Cardiology, Faculty of Medicine, Capital University, Egypt.

[3]Pharmacist at Badr University Hospital, Capital University, Egypt

[4]Lecturer of Clinical Pharmacy, Clinical Pharmacy Practice, Faculty of Pharmacy, Capital University, Egypt

Corresponding author*

Hadeer Mohamed Gamal Mohamed Fahmi Ali Saleh

ABSTRACT

Background: Obesity is a growing global health challenge, notably prevalent in Egypt, where it exacerbates cardiovascular risk. Enoxaparin, a low molecular weight heparin, is widely used for anticoagulation, yet standard dosing may not be optimal for obese patients due to altered pharmacokinetics. Limited local data exist on the clinical and economic implications of such dosing discrepancies in critically ill cardiovascular patients.

Objective: To assess the impact of obesity on the efficacy, safety, and ECHO (Economic, Clinical, and Humanistic Outcomes) of therapeutic enoxaparin in obese versus lean patients with cardiovascular diseases.

Methods: A prospective, observational cohort study was conducted at Badr University Hospital from December 2020 to December 2023. Fifty ICU/CCU patients receiving therapeutic enoxaparin (1 mg/kg SC every 12 hours) were grouped by BMI: obese (≥30 kg/m², n=25) and lean (<30 kg/m², n=25). Peak anti-factor Xa levels were measured 3–5 hours after the third dose. Secondary outcomes included oxygen therapy duration, hospital stay, INR, bleeding events, and total direct cost. Correlation and regression analyses explored predictors of anti-Xa activity.

Results: Obese patients had significantly lower anti-Xa levels (0.70 vs. 1.03 IU/mL, $p<0.001$), more frequent subtherapeutic exposure (32% vs. 0%), longer hospital stay (8.6 vs. 6.8 days), and higher costs (63.8 vs. 50.9 $\times 10^3$ LE). BMI was the only independent predictor of anti-Xa levels.

Conclusions: Standard enoxaparin dosing may lead to subtherapeutic anticoagulation in obese patients. Individualized dosing and anti-Xa monitoring are recommended to improve efficacy, reduce adverse outcomes, and optimize resource use

Keywords: Enoxaparin; Obesity; Anti-factor Xa; Cardiovascular diseases; Intensive care; ECHO model; Pharmacokinetics; Egypt

How to cite this article: Ebid AHIM, Gaafar A, Saleh HMGMF, Abdel-Motalebm SMM, Dosage Optimization of enoxaparin in the treatment of cardiovascular diseases in Egyptian obese patients,..Int J Drug Deliv Technol. 2026;16(15s): 871-879. DOI: 10.25258/ijddt.16.15s.97

Source of support: Nil.

Conflict of interest: None

INTRODUCTION

Cardiovascular diseases (CVDs) remain the leading cause of mortality globally, and Egypt is no exception, with ischemic heart disease accounting for over one-fifth of all deaths. Contributing significantly to this burden is the alarming rise in obesity, which now affects over 35% of the adult Egyptian population—ranking among the highest in the world **(1)**. Obesity is not merely a comorbid condition but a key modifier of drug pharmacokinetics and pharmacodynamics, especially in critically ill patients. This has profound implications for the use of anticoagulants like enoxaparin, a low molecular weight heparin (LMWH) commonly administered for the prevention and treatment of venous thromboembolism (VTE) and acute coronary syndromes (ACS) in ICU/CCU settings **(2)**.

Despite the broad use of enoxaparin and its predictable pharmacokinetic profile in general populations, clinical outcomes in obese patients remain inconsistent. International studies suggest that standard weight-based dosing (1 mg/kg every 12 hours) may lead to subtherapeutic anticoagulation in obese patients and supratherapeutic levels in lean individuals **(3)**. However, such findings are primarily based on Western populations, with significant underrepresentation of critically ill obese patients in Middle Eastern or Egyptian healthcare settings. Moreover, few studies have comprehensively evaluated the ECHO (Economic, Clinical, and Humanistic Outcomes) model in this context, which is crucial for health policy and cost-effectiveness analysis in resource-limited settings **(4, 5)**.

The novelty of this study lies in its integration of pharmacokinetic monitoring (anti-factor Xa levels) with

**Author for Correspondence: Hadeer Mohamed Gamal Mohamed Fahmi Ali Saleh*

clinical and economic outcomes to assess the appropriateness of standard enoxaparin dosing in an Egyptian ICU cohort. This is the first prospective study in Egypt to use anti-factor Xa activity as a biomarker to evaluate dosing efficacy and to link these levels with a multidimensional ECHO framework. It also proposes a locally validated regression model for dose individualization, which is currently lacking in national guidelines.

Given these gaps, we conducted a prospective, observational cohort study to assess how obesity influences the pharmacodynamics of therapeutic-dose enoxaparin, its clinical efficacy and safety, and associated healthcare costs in critically ill cardiovascular patients. This approach not only addresses a pressing clinical need but also has implications for future dosing guidelines and patient safety strategies.

Consequently, the aim of this study is to evaluate the impact of obesity on the efficacy, safety, and economic outcomes of therapeutic enoxaparin in ICU/CCU patients with cardiovascular diseases. Specifically, the study seeks to determine whether fixed weight-based dosing results in suboptimal anticoagulation in obese patients and whether BMI-based dose adjustment or anti-Xa monitoring should be considered to optimize therapy and reduce complications.

Patients and Methods

After ethical committee approval and written consents from the patients, this study was designed as a prospective, observational, controlled cohort study. It was conducted at the Intensive Care Unit (ICU) and Cardiovascular Care Unit (CCU) of Badr University Hospital, affiliated with Capital University **(Previously called Helwan University),** Cairo, Egypt, over a 3-year period from December 2020 to December 2023.

Patient Selection

Adult patients admitted to ICU/CCU with cardiovascular conditions and receiving therapeutic enoxaparin were screened for eligibility.

Inclusion Criteria

- Age ≥ 18 years
- Admission to ICU or CCU
- Receiving a therapeutic dose of enoxaparin (1 mg/kg every 12 hours)

Exclusion Criteria

Patients were excluded if they met any of the following criteria:

- Pregnancy or breastfeeding
- Active malignancy or recent surgery
- Severe hepatic or renal impairment
- Known bleeding disorders (e.g., hemophilia, thrombocytopenia)
- Infective endocarditis or peptic ulcer disease
- Active bleeding, retinopathy, or any condition requiring modified anticoagulation dosing

Treatment and Grouping

All included patients received enoxaparin sodium (Clexane® 80 mg/0.8 mL, Sanofi-Aventis, France) subcutaneously at a fixed treatment dose of 1 mg/kg every 12 hours, per hospital protocol. Based on body mass index (BMI), patients were stratified into:

- **Lean Group (Gp-L):** BMI < 30 kg/m²
- **Obese Group (Gp-O):** BMI ≥ 30 kg/m²

Data Collection and Investigations

Upon admission, detailed clinical history and physical examinations were performed. Data collected included:

- Demographics (age, sex)
- Comorbidities (e.g., hypertension, diabetes)
- Laboratory results:

• Complete Blood Count (CBC)
• Liver and kidney function tests
• International Normalized Ratio (INR).

Outcome Measures (ECHO Framework)

The study adopted the ECHO model (Economic, Clinical, and Humanistic Outcomes) to assess treatment impact.

Primary Outcome

- **Peak anti-factor Xa activity (IU/mL):**

Measured 3–5 hours after the third dose at steady state using a chromogenic anti-Xa assay (Sysmex CN-6000 analyzer).

- **Therapeutic Ranges:**

•Subtherapeutic: <0.5 IU/mL
•Therapeutic: 0.5–1.0 IU/mL
• Supratherapeutic: >1.0 IU/mL

Secondary Outcomes

1. Duration of supplementary oxygen therapy (days)
2. Length of hospital stay (days)
3. INR at discharge
4. Incidence of bleeding events (minor, GIT, urinary)
5. Occurrence of deep vein thrombosis (DVT)
6. In-hospital mortality

Economic Outcome

- **Total Direct Hospital Cost** per patient (in $\times 10^3$ Egyptian Pounds), including:
  1. ICU/CCU bed-day charges
  2. Medication costs (enoxaparin and others)
  3. Laboratory tests (including anti-Xa assays)
  4. Imaging and diagnostic procedures
  5. Consumables and interventions

Humanistic Outcomes

- Baseline mobility status
- Need for supplementary oxygen at admission

Sample size calculation

The sample size was calculated based on the primary outcome, peak anti-factor Xa activity (IU/mL), comparing obese (BMI ≥30 kg/m²) and lean patients (BMI <30 kg/m²) receiving therapeutic enoxaparin. Assuming a clinically relevant difference of 0.30 IU/mL in mean anti-factor Xa levels between groups, with an estimated standard deviation of 0.30 IU/mL (large effect size, Cohen's d ≈ 1.0), a two-sided α error of 0.05 and a study power of 80% (β = 0.20), the minimum required sample size was 23 patients per group for an independent-samples t-test.

To allow for potential dropouts, missing data, and to ensure adequate power for regression analysis, the target sample size was increased to 25 patients per group, yielding a maximum total sample of 50 adult patients.

Statistical Analysis

Data were analyzed using IBM SPSS Statistics version 28.0. Quantitative variables were expressed as mean ± SD and compared using independent t-tests or ANOVA, while qualitative variables were compared using Chi-square or Fisher's exact tests. Pearson correlation assessed variable relationships. Linear regression analysis was performed to identify independent predictors of anti-factor Xa activity. A p-value ≤ 0.05 was considered statistically significant.

Results

During the study period, **70 adult patients** admitted to the ICU or CCU with cardiovascular diseases were assessed for eligibility. Of these, **20 patients were excluded**:
– Twelve patients (n = 12) did not meet the inclusion/exclusion criteria.
– Eight patients (n = 8) declined to participate.
A total of **50 patients** were therefore enrolled and included in the study. Eligible patients were then categorized according to BMI into two groups:
– **Obese group (Gp-O):** 25 patients with BMI ≥30 kg/m².
– **Lean group (Gp-L):** 25 patients with BMI <30 kg/m².
All enrolled patients received therapeutic-dose enoxaparin and completed follow-up. No patients were lost during the study, and **all 50 patients were included in the final statistical analysis**.

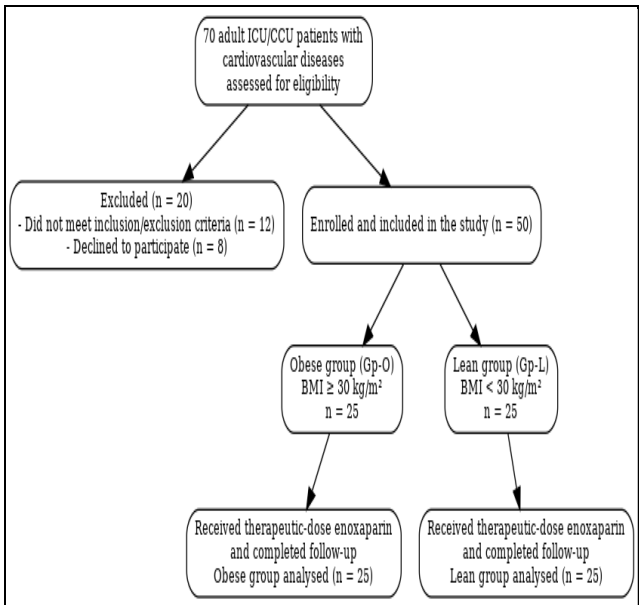

Figure (1): Patient enrollment and follow-up flow diagram.

Figure (1) summarizes the patient flow throughout the study. Of 70 ICU/CCU patients assessed for eligibility, 20 were excluded, leaving 50 patients who were enrolled and completed follow-up. Patients were allocated into two equal groups based on BMI (25 obese and 25 lean), and all received therapeutic-dose enoxaparin with no loss to follow-up. This ensures a clear and unbiased comparison between the study groups.

Table 1. Demographic characteristics between the studied groups.

Variables		Obese group (Total=25)	Lean group (Total=25)	p-value
Age (years)	Mean ±SD	49.1±8.1	47.5±7.9	^0.483
	Range	33.0–65.0	34.0–64.0	
BMI (kg/m²)	Mean ±SD	36.6±2.4	22.4±1.6	^<0.001*
	Range	30.6–40.3	18.7–24.8	
Sex, (n, %)	Male	15 (60.0%)	16 (64.0%)	#0.771
	Female	10 (40.0%)	9 (36.0%)	
Smoking, (n, %)		10 (40.0%)	11 (44.0%)	#0.774
Hypertension, (n, %)		14 (56.0%)	15 (60.0%)	#0.774
Diabetes mellitus, (n, %)		5 (20.0%)	3 (12.0%)	§0.702
Clopidogrel, (n, %)		8 (32.0%)	7 (28.0%)	#0.758
NSAID, (n, %)		2 (8.0%)	4 (16.0%)	§0.667

BMI: Body mass index. ^Independent t-test. #Chi square test. §Fisher's Exact test. *Significant.

Table 1 shows that there were no statistically significant differences between obese and lean groups regarding age, sex, smoking status, hypertension, diabetes mellitus, clopidogrel use, or NSAID use (all p > 0.05). As expected, BMI was significantly higher in the obese group than in the lean group (p < 0.001), confirming the appropriate separation of the two BMI categories.

Table 2. Clinical characteristics at admission between the studied groups.

Variables		Obese group (Total =25)	Lean group (Total =25)	p-value
Cause of admission , (n, %)	Acute coronary syndrome	11 (44.0%)	12 (48.0%)	§0.651
	Cerebrovascular disease	8 (32.0%)	10 (40.0%)	
	Peripheral arterial disease	6 (24.0%)	3 (12.0%)	
Need for supplementary oxygen, (n,%)		8 (32.0%)	9 (36.0%)	#0.765
Mobility, (n, %)		16 (64.0%)	17 (68.0%)	#0.765
Hemoglobin (gm/dL)	Mean±SD	12.1±0.9	12.0±1.0	^0.741
	Range	10.6–13.7	9.3–13.5	
Platelets (gm/dL)	Mean±SD	383.2±66.5	405.3±66.2	^0.243
	Range	254.0–502	293.0–550.0	
Baseline INR	Mean±SD	1.11±0.09	1.12±0.12	^0.788
	Range	0.90–1.30	1.00–1.30	

^Independent t-test. #Chi square test. §Fisher's Exact test.

As demonstrated in Table 2, the cause of admission (acute coronary syndrome, cerebrovascular disease, or peripheral arterial disease) was comparable between obese and lean patients, with no statistically significant differences. The need for supplementary oxygen at admission, baseline mobility, hemoglobin level, platelet count, and baseline INR were also similar between the two groups ($p > 0.05$), indicating comparable initial clinical and laboratory status.

Table 3. Anti-Factor Xa activity between the studied groups

Variables		Obese group (Total =25)	Lean group (Total =25)	p-value
Anti-Factor Xa (IU/ml)	Mean±SD	0.70±0.33	1.03±0.22	^<0.001*
	Range	0.13–1.47	0.64–1.44	
Anti-Factor Xa grade , (n, %)	Subtherapeutic	8 (32.0%)a	0 (0.0%)b	§<0.001*
	Therapeutic	16 (64.0%)a	18 (72.0%)a	
	Supratherapeutic	1 (4.0%)a	7 (28.0%)b	

^Independent t-test. §Fisher's Exact test. *Significant. Homogenous grades across groups had the same symbol "a,b" based on post hoc Bonferroni test.

Table 3 shows that mean anti-factor Xa activity was significantly lower in the obese group compared with the lean group (0.70 ± 0.33 vs. 1.03 ± 0.22 IU/mL, $p < 0.001$). Subtherapeutic anti-factor Xa levels were significantly more frequent in obese patients (32.0% vs. 0.0%), whereas supratherapeutic levels were significantly more frequent in lean patients (28.0% vs. 4.0%; $p < 0.001$). The proportion of patients within the therapeutic range was similar between groups. These findings suggest that the standard 1 mg/kg twice-daily dose may be relatively low for obese patients and relatively high for lean patients.

Table 4. Clinical outcomes between the studied groups.

Variables		Obese group	Lean group	p-value
Supplementary oxygen (days)	Sample	Total= 8	Total= 9	^0.029*
	Mean ±SD	4.3±1.7	2.7±1.0	
	Range	2.0–7.0	1.0–4.0	
		Total= 25	Total= 25	
Hospital stay (days)	Mean ±SD	8.6±2.5	6.8±2.4	^0.018*
	Range	5.0–15.0	3.0–12.0	
Discharge INR	Mean ±SD	1.29±0.14	1.42±0.13	^0.002*
	Range	1.00–1.50	1.20–1.70	
Bleeding (minor), (n, %)		2 (8.0%)	4 (16.0 %)	§0.667
Bleeding (GIT), (n, %)		1 (4.0%)	3 (12.0 %)	§0.609
Bleeding (Urinary), (n, %)		1 (4.0%)	2 (8.0%)	§0.999
DVT, (n, %)		0 (0.0%)	0 (0.0%)	NA
Mortality (in hospital), (n, %)		3 (12.0%)	2 (8.0%)	§0.999

NA: Not applicable. ^Independent t-test. §Fisher's Exact test.

As presented in Table 4, the duration of supplementary oxygen therapy was significantly longer in obese patients compared with lean patients (4.3 ± 1.7 vs. 2.7 ± 1.0 days, p = 0.029). Hospital stay was also significantly prolonged in the obese group (8.6 ± 2.5 vs. 6.8 ± 2.4 days, p = 0.018). Discharge INR was significantly higher in the lean group (1.42 ± 0.13 vs. 1.29 ± 0.14, p = 0.002).

Bleeding events (minor, gastrointestinal, or urinary) were numerically more frequent in the lean group, although these differences were not statistically significant. No cases of DVT were observed in either group, and in-hospital mortality was numerically higher in obese patients but without statistical significance.

Table 5. Economic outcome (Cost (x10^3 LE) between the studied groups).

Variables	Obese group (Total=25)	Lean group (Total=25)	p-value
Mean±SD	63.8±19.3	50.9±17.5	^0.016*
Range	36.5–116.5	21.9–87.6	

^Independent t-test. *Significant.

Table 5 demonstrates that the mean total direct hospital cost (×10³ LE) was significantly higher in obese patients than in lean patients (63.8 ± 19.3 vs. 50.9 ± 17.5, p = 0.016). This reflects the increased healthcare resource utilization associated with obesity, likely driven by the longer duration of oxygen requirement and hospital stay in the obese group.

Table 6. Correlations of factor Xa activity level among the studied groups.

Variables		Obese group (Total=25)	Lean group (Total=25)
Age (years)	R	0.321	-0.080
	p-value	0.118	0.703
BMI (kg/m^2)	R	-0.702	-0.646
	p-value	**<0.001***	**<0.001***
Supplementary oxygen (days)	R	-0.774	-0.780
	p-value	**0.024***	**0.013***
Hospital stay (days)	R	-0.682	-0.507
	p-value	**<0.001***	**0.010***
Discharge INR	R	0.572	0.661
	p-value	**0.003***	**<0.001***

BMI: Body mass index. Pearson correlation test. *Significant.

Table 6 shows that anti-factor Xa activity had a significant negative correlation with BMI in both obese and lean groups (p < 0.001), indicating that higher BMI is associated with lower anti-factor Xa levels. Anti-factor Xa levels also correlated negatively with the duration of supplementary oxygen and hospital stay, and positively with discharge INR in both groups. Age did not show a significant correlation with anti-factor Xa activity.

Table 7. Comparison according to demographic and clinical characteristics at admission regarding factor Xa activity level (IU/ml) among the studied groups.

Variables		Obese group (Total=25)	Lean group (Total=25)
Sex	Male	0.63±0.30	1.06±0.23
	Female	0.81±0.38	0.97±0.19
	^p-value	0.177	0.316
Smoking	Yes	0.63±0.32	0.97±0.19
	No	0.75±0.34	1.08±0.24
	^p-value	0.396	0.214
Hypertension	Yes	0.68±0.33	1.04±0.19
	No	0.73±0.35	1.01±0.26
	^p-value	0.723	0.734
Diabetes mellitus	Yes	0.73±0.25	1.00±0.37
	No	0.69±0.35	1.03±0.21
	^p-value	0.854	0.814
Cause of admission	Coronary artery disease	0.63±0.26	1.05±0.24
	Cerebrovascular disease	0.88±0.38	0.99±0.19
	Peripheral arterial disease	0.58±0.34	1.08±0.27
	#p-value	0.163	0.772
Mechanical ventilation at admission	Yes	0.70±0.40	1.11±0.24
	No	0.70±0.32	0.98±0.20
	^p-value	0.964	0.17

^Independent t-test. #ANOVA test.

Table 8. Comparison according to clinical outcomes regarding factor Xa activity level among the studied groups.

Variables		Obese group (Total=25)	Lean group (Total=25)
Bleeding (minor)	Yes	1.28±0.27	1.31±0.19
	No	0.65±0.29	0.97±0.18
	^p-value	**0.007***	**0.003***
Mortality	Yes	0.53±0.14	1.14±0.15
	No	0.72±0.35	1.02±0.22
	^p-value	0.363	0.487

^

Independent t-test. #ANOVA test. *Significant.

Table 9 demonstrates that, in both obese and lean groups, patients who experienced minor bleeding had significantly higher anti-factor Xa levels compared with those without bleeding ($p = 0.007$ and $p = 0.003$, respectively). In contrast, anti-factor Xa levels did not differ significantly between survivors and non-survivors. These findings support a potential association between supratherapeutic anti-factor Xa levels and bleeding risk.

Table 9. Linear regression for factors affecting factor Xa activity among the study groups.

Factors	B	SE	p-value	95% CI	R^2
Obese group					
Constant	4.474	0.758	**<0.001***	2.707–5.81	0.493
BMI	-0.098	0.021	**<0.001***	-0.141–-0.055	
Lean group					
Constant	2.993	0.485	**<0.001***	1.989–3.998	0.417
BMI	-0.088	0.022	**<0.001***	-0.132–-0.043	

β: Regression coefficient. SE: Standard error. *Significant. CI: Confidence interval. R^2: Coefficient of determination

As summarized in Table 9, after entering demographic and clinical variables into the linear regression models, BMI remained the only independent predictor of anti-factor Xa activity in both obese and lean groups. In obese patients, the model was:
Anti-factor Xa activity (IU/mL) = 4.474 − 0.098 × BMI (kg/m²) (R^2 = 0.493).
In lean patients, the model was:
Anti-factor Xa activity (IU/mL) = 2.993 − 0.088 × BMI (kg/m²) (R^2 = 0.417).
This indicates that each 1 kg/m² increase in BMI is associated with an approximate decrease of 0.098 IU/mL and 0.088 IU/mL in anti-factor Xa levels in obese and lean patients, respectively.

Discussion

Obesity represents a major and escalating public health concern in Egypt. Recent epidemiological data estimate that adult obesity prevalence has surpassed 36–39%, placing Egypt among the countries with the highest global rates **(7, 8).** This growing burden has been directly linked to increased cardiovascular morbidity, prolonged hospital stays, and rising healthcare costs. Several local studies have reported that obese patients—particularly those in critical care—experience worse clinical outcomes, including extended ICU admissions, higher incidence of thromboembolic events, and elevated resource utilization **(9, 10).** Despite the significance of these findings, there remains a critical lack of local data regarding optimal enoxaparin dosing or the role of anti-factor Xa monitoring in this high-risk population.

Enoxaparin, a low molecular weight heparin (LMWH), is a cornerstone of anticoagulation therapy in acute coronary syndrome (ACS), venous thromboembolism (VTE), and intensive care settings. It is commonly dosed at 1 mg/kg

every 12 hours based on total body weight. However, obesity alters key pharmacokinetic parameters such as drug absorption, volume of distribution, and clearance, potentially undermining the safety and efficacy of this standard dosing strategy. Several international studies have demonstrated that obese patients frequently fail to achieve therapeutic anti-factor Xa levels, instead showing a tendency toward subtherapeutic anticoagulation even with weight-adjusted regimens **(11, 12).** Given these concerns, it becomes essential to reassess the appropriateness of fixed dosing strategies in this patient subgroup, especially within Egyptian ICU settings where tailored data are lacking.

Our prospective cohort study directly addresses this evidence gap by evaluating the pharmacodynamic response to therapeutic-dose enoxaparin in obese versus lean ICU patients with cardiovascular disease. Specifically, we assessed anti-factor Xa activity at steady state and correlated these levels with clinical, economic, and humanistic outcomes. This study represents the first pharmacoeconomic evaluation in Egypt linking obesity-related pharmacokinetic variability with real-world enoxaparin performance.

Consistent with global literature, our findings reveal that obese patients had significantly lower peak anti-factor Xa activity compared to lean patients, despite receiving the same weight-based therapeutic dose. A notable 32% of obese patients exhibited subtherapeutic anti-Xa levels, while supratherapeutic levels were more frequent in lean patients. These data support the hypothesis that standard dosing fails to account for the altered drug disposition seen in obesity, potentially compromising anticoagulant efficacy. Furthermore, linear regression analysis confirmed that body mass index (BMI) was the sole independent predictor of anti-factor Xa variability, explaining nearly 50% of the variance in obese patients. This correlation aligns with established pharmacokinetic theories, which attribute reduced drug exposure in obesity to increased clearance and altered tissue distribution **(13).**

Although prior Egyptian research has documented the clinical consequences of obesity in ICU populations—such as prolonged ventilation duration, increased hypoxemia risk, and higher healthcare costs—none have explicitly linked these outcomes to pharmacodynamic markers like anti-factor Xa. Our study uniquely demonstrates that subtherapeutic anti-Xa levels may underlie many of the poor outcomes seen in obese patients receiving standard enoxaparin dosing. This represents a novel contribution to the local literature and emphasizes the need for individualized anticoagulation strategies in Egyptian critical care settings.

Clinical and Pharmacodynamic Implications

Our study revealed a clear association between lower anti-factor Xa levels and adverse clinical outcomes in obese patients receiving standard therapeutic doses of enoxaparin. Specifically, subtherapeutic anti-Xa levels were linked to significantly longer durations of oxygen therapy, extended ICU and hospital stays, increased total healthcare costs, and a trend toward higher in-hospital mortality. Conversely, patients with supratherapeutic anti-Xa levels—primarily from the lean group—exhibited a higher frequency of bleeding complications. These findings reinforce the pharmacodynamic principle that inadequate anticoagulation due to subtherapeutic anti-Xa exposure may result in thrombotic complications and clinical deterioration, while excessive anticoagulation increases bleeding risk. Moreover, the observed inverse correlation between anti-Xa activity and hospital length of stay highlights the importance of achieving and maintaining optimal anticoagulant levels, consistent with prior international studies **(14, 15).**

Economic and Humanistic Outcomes (ECHO Framework)

Incorporating the ECHO (Economic, Clinical, and Humanistic Outcomes) framework provided a multidimensional evaluation of enoxaparin therapy. Obese patients not only experienced worse clinical outcomes but also demonstrated significantly higher total direct hospital costs, greater resource utilization—including prolonged ICU stays and extended oxygen requirements—and poorer functional status on admission. The cost difference, approximately 13,000 Egyptian Pounds higher in obese patients, aligns with global pharmacoeconomic data suggesting that obesity contributes an additional 20–40% in medical costs per hospitalization **(16).** Notably, this is the first Egyptian study to integrate clinical efficacy, laboratory pharmacodynamics (anti-Xa), economic burden, and functional status into a single comprehensive framework for assessing LMWH therapy in high-risk patients.

Mechanistic Interpretation and Clinical Relevance

Taken together, these findings establish a consistent mechanistic cascade: higher BMI leads to lower anti-factor Xa activity, which correlates with longer durations of oxygen dependency and hospital stay, ultimately resulting in increased healthcare expenditures. This causal sequence substantiates the clinical need for routine anti-Xa monitoring in obese patients and supports the move toward individualized dosing protocols. The study also proposes a rationale for the development of practical bedside dosing nomograms based on BMI or predicted anti-Xa levels, which could enhance both safety and efficacy.

Comparison with International Evidence

The results of this study align well with international trials that have investigated empiric dose modifications for LMWH in obese populations. For example, reducing the enoxaparin dose to 0.75 mg/kg in patients with a BMI >40 kg/m² has been shown to improve therapeutic target attainment **(17).** Similarly, several studies have demonstrated that higher prophylactic doses more consistently achieve anti-Xa targets **(18, 19)**. Furthermore, supratherapeutic anti-Xa levels have been associated with an increased bleeding risk **(20)**, which was also observed in the lean subgroup of our study. By incorporating a locally validated regression model to predict anti-Xa levels from BMI, this study contributes a novel tool that may guide exploratory individualized dosing strategies tailored to Egyptian patients.

Strengths and Limitations

This study possesses several notable strengths. It is the first prospective Egyptian cohort to examine the pharmacodynamic effects of obesity on enoxaparin therapy within an integrated ECHO framework. The study design was prospective with standardized sampling at steady state, zero loss to follow-up, and inclusion of both clinical and economic outcomes. Additionally, regression modeling confirmed BMI as a robust, independent predictor of anti-Xa variability.

However, the study is not without limitations. It was conducted at a single center with a modest sample size, which may limit generalizability. Only peak anti-Xa levels were measured, without assessment of trough levels or time-to-peak variability. Furthermore, certain clinical confounders—such as presence of sepsis, use of vasopressors, or fluid overload—were not stratified, which may influence pharmacokinetics and outcomes.

Overall Interpretation and Future Direction

Collectively, the data presented here strongly support that fixed, weight-based enoxaparin dosing is suboptimal in obese Egyptian ICU patients with cardiovascular disease. The BMI-driven variability in anti-factor Xa activity leads to meaningful differences in clinical and economic outcomes. These findings advocate for anti-Xa–guided dose adjustment and provide the groundwork for the development of national dosing protocols and individualized anticoagulation strategies in Egypt. Future research should aim to validate these findings in larger, multicenter cohorts and explore dose optimization algorithms that ensure both safety and cost-effectiveness in high-risk populations.

CONCLUSION

This prospective cohort study highlights the inadequacy of standard fixed weight-based enoxaparin dosing (1 mg/kg every 12 hours) in obese critically ill cardiovascular patients. Obesity was significantly associated with lower anti-factor Xa activity, more frequent subtherapeutic levels, prolonged oxygen use, longer hospital stay, and higher healthcare costs. BMI emerged as the sole independent predictor of anti-factor Xa levels in both obese and lean patients, underscoring the need for individualized dosing strategies.

Regression models demonstrated a strong inverse relationship between BMI and anti-Xa activity, supporting routine anti-Xa monitoring and dose adjustment in patients with BMI ≥ 30 kg/m². A proposed formula for exploratory dose individualization based on predicted anti-Xa levels offers a promising tool but requires further validation in larger randomized trials before clinical adoption.

Anti-factor Xa monitoring should be routinely implemented in obese patients (BMI ≥ 30 kg/m²) receiving therapeutic enoxaparin, especially in critical care. Dose adjustment based on anti-Xa levels is advised to achieve optimal anticoagulation and minimize bleeding risk. Future randomized studies are needed to compare standard versus individualized dosing strategies. Larger multicenter trials should validate BMI-based prediction models and develop practical dosing tools. Adoption of the ECHO model is encouraged to assess clinical, economic, and humanistic outcomes. This study provides preliminary support for dose individualization, warranting further confirmation in larger cohorts.

List of Abbreviations

- **ACS** – Acute Coronary Syndrome
- **BMI** – Body Mass Index
- **CBC** – Complete Blood Count
- **CCU** – Cardiovascular Care Unit
- **CVD** – Cardiovascular Diseases
- **DVT** – Deep Vein Thrombosis
- **ECHO** – Economic, Clinical, and Humanistic Outcomes
- **ICU** – Intensive Care Unit
- **INR** – International Normalized Ratio
- **LMWH** – Low Molecular Weight Heparin
- **LE** – Egyptian Pounds
- **SC** – Subcutaneous
- **VTE** – Venous Thromboembolism

Ethical Considerations

This study was approved by the Ethics Committee of the Faculty of Pharmacy, Capital University (previously called Helwan University) (Protocol No. 06H2020). All participants provided written informed consent before enrollment. The study was conducted in compliance with the Declaration of Helsinki and is registered under Capital University Identification Number 9144056.

Acknowledgment

The authors gratefully acknowledge the medical and nursing staff of Badr University Hospital, Capital University, for their assistance in data collection and patient care. We also extend our thanks to the biochemistry lab team for their support in conducting the anti-factor Xa assays.

Conflicts of Interest

The authors declare no conflicts of interest related to this study.

Confidentiality of Data

All patient data were anonymized and treated with strict confidentiality. Data were used exclusively for the purpose of this research and stored securely in compliance with institutional data protection policies.

Financing Support

This study did not receive any external funding. All expenses related to data collection, laboratory testing, and statistical analysis were covered by the authors

REFERENCE

1. Nofal MN, Wadi WI, Yousef AJ, Rashdan MZ, Alkhasawneh MH, Dwairi RN, et al. Single-dose enoxaparin for portomesenteric venous thrombosis prophylaxis after sleeve gastrectomy. Ann Afr Med. 2024 Jan 1;23(1):46–52.
2. Baghaghow AS, Elahwal LM. Low dose aspirin versus low dose aspirin plus omega 3 versus low molecular weight heparin in treatment of unexplained recurrent miscarriage. Int J Health Sci. 2022;6(S5):3682–7.

3. Sahraei Z, Eshraghi A, Barati S. Evaluating anti-factor Xa levels in patients with augmented renal clearance receiving enoxaparin prophylaxis: An exploratory pilot study. J Res Pharm Pract. 2025 Jan 1;14(1):35–8.
4. Kasprzak JD, Gorczyca-Głowacka I, Sobczak-Kaleta M, Barylski M, Drożdż J, Filipiak KJ, et al. Pharmacotherapy of heart failure AD 2023. Expert opinion of Working Group on Cardiovascular Pharmacotherapy, Polish Cardiac Society. Kardiol Pol. 2023;81(5):537–56.
5. John S, Wilkinson M, Ho KM. Monitoring anti-Xa levels to optimize low-molecular-weight-heparin thromboprophylaxis in high-risk hospitalized patients: a stratified meta-analysis. Angiology. 2024 Mar;75(3):249–66.
6. Abuelsoud NN, Abdelraouf FH. The effect of genetic polymorphisms, drug-disease and drug-drug interactions on hypertension control in Egyptian patients. Res J Pharm Technol. 2025 Feb 1;18(2):839–51.
7. Afifi M, El-Sayed N, Abdel-Rahman W. Obesity trends and associated cardiovascular risks in Egypt: a population-based analysis. J Public Health. 2022;44:1123–32.
8. NCD Risk Factor Collaboration (NCD-RisC). Worldwide trends in body-mass index, overweight, and obesity. Lancet. 2021;397:191–212.
9. Abdul-Razek H, Ahmed M, Hassan A. Impact of obesity on ICU outcomes among critically ill Egyptian patients. Egypt J Crit Care Med. 2019;7:45–52.
10. El-Feky M, Abdelwahab S, El-Mesery M. Obesity and prolonged ICU stay in Egyptian cardiac patients. Egypt J Bronchol. 2020;14:26.
11. Tahaineh L, Edaily SM, Gharaibeh SF. Anti-factor Xa levels in obese patients receiving enoxaparin for treatment and prophylaxis indications. Clin Pharmacol Adv Appl. 2018;10:63–70.
12. Berger JS, Rathbun S, Wilson A. Evaluation of enoxaparin dosing and anti-Xa monitoring in obese adults. Thromb Res. 2023;225:1–7.
13. Lee Y, Lee S, Lee J. Pharmacokinetics of enoxaparin in obese adults: absorption and clearance considerations. J Clin Pharm Ther. 2015;40:340–6.
14. Rostas JW, Brevard SB, Simmons JD. Predictors of enoxaparin dosing variability in trauma patients. J Trauma Acute Care Surg. 2015;79:870–5.
15. Dennis DM, Bharat C, Paterson T. Prevalence of obesity and the effect on length of mechanical ventilation and length of stay in intensive care patients: a single site observational study. Aust Crit Care. 2017;30(3):145–50.
16. Biener A, Cawley J, Meyerhoefer C. The impact of obesity on medical care costs and labor market outcomes in the US. Clin Chem. 2018;64(1):108–17.
17. Lalama JT, Brumfield JL, Slaughter RL. Adjusted enoxaparin dosing in obesity: impact on therapeutic anti-Xa levels. Int J Clin Pharm. 2015;37:1239–45.
18. Simone EP, Madan AK, Tichansky DS. Comparison of two enoxaparin dosing regimens in bariatric surgery patients. Surg Obes Relat Dis. 2008;4:625–9.
19. Freeman A, Horner T, Pendleton RC, Rondina MT. Prospective comparison of three enoxaparin dosing regimens to achieve target anti-factor Xa levels in hospitalized, medically ill patients with extreme obesity. Am J Hematol. 2012;87(7):740–3.
20. Deal EN, Hollands JM, Riney JN. Bleeding risk and supratherapeutic anti-factor Xa levels in obese patients receiving enoxaparin. Pharmacotherapy. 2011;31:19–26