

**DRUG UTILIZATION EVALUATION OF LOW MOLECULAR WEIGHT HEPARIN IN A  
TERTIARY CARE TEACHING HOSPITAL****Binu Mathew\*, Nimmy N. John, Lovely Panavila and H. Doddayya**

Department of Pharmacy Practice, NET Pharmacy College, Raichur, Karnataka, India.

**\*Corresponding Author: Binu Mathew**

Department of Pharmacy Practice, NET Pharmacy College, Raichur, Karnataka, India.

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**ABSTRACT**

Low molecular weight heparins (LMWH) have achieved poly therapeutic drug status and additional indications for their use. Therefore, it is necessary to evaluate the usage of LMWHs in the hospital settings. The main objective of the study was to analyse the prescribing habits of LMWH for their appropriateness and to promote its rational use. The prospective study was carried out in a total of 200 patients treated with LMWH in hospital. Patients receiving unfractionated heparins and other anticoagulant drugs in the hospital were excluded. Details of in patient who were treated with LMWHs were collected from patient files. Evaluation of demographic data revealed that 70.5% (n=141) were males while 29.5% (n=59) were females. A high percentage of patients aged between 53 -73 years were found in the study population. Laboratory monitoring analysis shows that haemoglobin test was done for 91% (182) followed by APTT monitoring (73%) and INR 61% (122) of the total populations. The most commonly prescribed LMWH was enoxaparin (82.5%). The most prominent indication for which it was prescribed was Ischemic Heart Disease (37.5%). Aspirin was the most other antiplatelet drug prescribed along with LMWH for maximum number of patients 31% (n=62). In cost analysis, it was found that maximum number of patients was in 5000-1000 Rs range about 42.5%. During the study period, APTT monitoring was found to be inappropriate according to the LMWH prescribing guidelines. Also implementation of guidelines for the use of LMWHs would promote the rational use of LMWHs.

**KEYWORDS:** APTT, Enoxaparin, Heparin, Guidelines, LMWH, UFH.**INTRODUCTION**

LMWH are currently being developed for several newer indications, including management of ischemic and thrombotic stroke, treatment of unstable angina and related coronary syndromes, prophylaxis of thrombosis during interventional cardio vascular procedures such as stenting, atherectomy and thrombolysis, management of transplant associated venocclusive disorders and management of cancer associated thrombosis. These agents have achieved poly therapeutic drug status and additional indications for their use are continually explored.<sup>[1]</sup>

Main advantages of LMWH therapy are ability to administer by subcutaneous injection resulting reduced hospital stay and a lower incidence of heparin induced Thrombocytopenia (HIT) and possibly a lower risk of Osteopenia. Half-life of LMWH is two to four times longer, up to 5 hours. This extend action allows LMWHs to be administered once or twice daily for a sustained 24-hour effect.<sup>[2,3]</sup>

Although outpatient LMWH therapy requires trained medical personal to educate patients and monitor outpatient care, these expenses do not exceed the cost of

inpatient care. In various pharmacoeconomic studies, the economic and points like drugs costs, drug preparation costs, etc LMWH treatment is more cost effective than UFH treatment in various clinical conditions.<sup>[4,5]</sup>

The major risks of LMWH therapy are bleeding, osteoporosis in long term use, heparin induced thrombocytopenia, hyperkalemia and altered hepatic function. The optimal utilization of LMWH is important to minimizing the development of bleeding, osteoporosis, hyperkalemia, thrombocytopenia and altered hepatic function.<sup>[6]</sup>

So appropriate monitoring is necessary because, the anticoagulant response to heparin varies greatly over time between patients as well as in individual patients. The optimal utilization of LMWHs is important in minimizing bleeding and cost of treatment. It is therefore, necessary to evaluate the usage of Low Molecular weight Heparins in the hospital settings to improve quality of use of these agents by proper utilization.

In this context, the study entitled "Drug utilization evaluation of Low molecular weight heparin in a tertiary

care teaching hospital” was undertaken to analyze prescription pattern, monitoring practices of heparin.

**MATERIALS AND METHODS**

The study was conducted in Navodaya Medical College Hospital and Research Centre at Raichur. This prospective study was designed to evaluate the usage pattern of LMWH in adults for their appropriateness. The study was conducted over a period of six months from August 2016 to January 2017. The consent for conducting the study was obtained from the Institutional Ethics Committee (IEC) of the hospital.

The study population include 200 subjects. The data was collected from various sources such as patient’s case reports, treatment charts and also through direct patient interview. The study criteria involves:

**Inclusion Criteria:** Patients who received Low molecular weight heparins in the hospital.

**Exclusion Criteria:** Patients receiving unfractionated heparins and other anticoagulant drugs in the hospital.

Details of in patient who were treated with LMWHs were collected from Inpatient pharmacy (IP) pharmacy and patient files in wards. A well designed data entry form was used for collecting data for this study. Data collection included patient details, laboratory investigations, LMWHs prescribed, other drugs prescribed.

**RESULTS AND DISCUSSION**

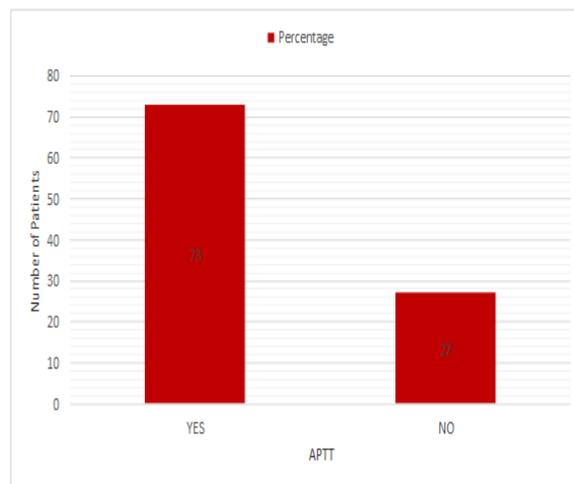
This study was conducted in order to evaluate and improve the rate of appropriate use of Low Molecular Weight Heparins. Gender distribution showed that male patients (70.5%) far exceeded than female patients (29.5%) in the study. These findings are similar to the study carried out by Fanak Fahimi et al<sup>[7]</sup> where the male population predominate the female population. Age group analysis of the patients showed that in the study, the most prominent age groups were ‘53-73’ which constitutes 50.5%(n=101) followed by 32-52, which constitutes 31% (n= 62).

Laboratory monitoring analysis shows, Haemoglobin test was done for 91% (182) of the total populations, followed by APTT monitoring (73%) and INR 61% (122) of the total populations as shown in **table 1, fig 1 & 2**. The most significant result is that, APTT monitoring was done for 73% of the total prescriptions as shown in **figure 2**. APTT monitoring is precautionary to ensure the safety of LMWHs therapy. These findings are not similar to the study carried out by Fanak Fahimi et al.<sup>[7]</sup> The need for frequent laboratory tests, i.e, activated partial thromboplastin time (APTT), the time spent on these tests, as well as the staff involved from patient’s bedside to laboratory, could result in extra costs and potential complications in patients. APTT monitoring was recommended for UFH therapy. In the case of

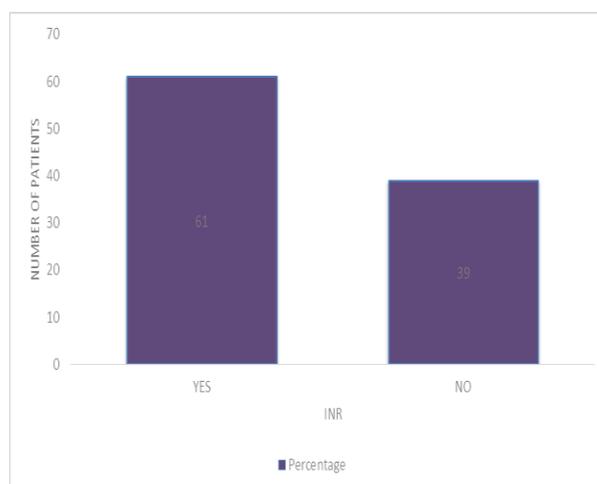
LMWH therapy daily monitoring of APTT is not recommended. In the study it was found that 73% of APTT monitoring. So these will further increase the laboratory monitoring, this is brought to the notice of prescribing physicians in the hospital.<sup>[7]</sup>

**Table I: Haemoglobin wise distribution from the total population (n=200).**

HAEMOGLOBIN	NUMBER OF PATIENTS
Yes	182(91%)
No	18 (9%)



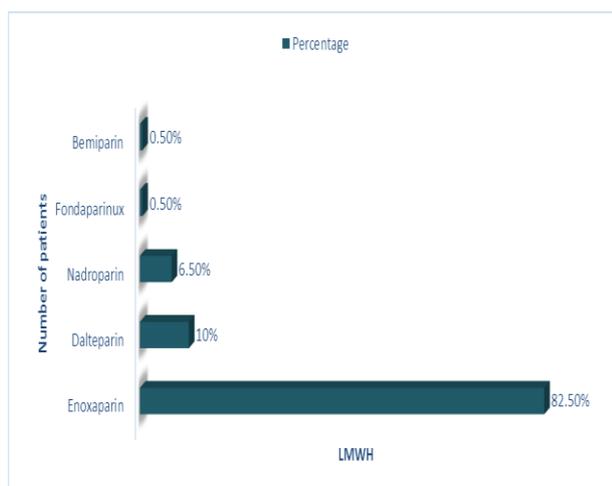
**Figure I: Activated partial thromboplastin time (APTT) wise distribution from the total population (n=200).**



**Figure II: International Normalised Ratio (INR) Wise Distribution from the Total Population (N=200).**

In LMWH prescription analysis, the most prescribed LMWH was Enoxaparin constitute 82.5%(165) followed by dalteparin constitute only 10%(20). Nadroparin 6.5% (13), Fondoparinux 0.5%(1) and Bemiparin 0.5%(1). (**Fig 3**). The most prescribed LMWH was Enoxaparin which were approved by US-FDA. Another LMWH, Dalteparin which was prescribed 10%(20), were also US-FDA approved. So the US-FDA approved Low

Molecular Weight Heparin were prescribed in this hospital.<sup>[8,9]</sup>



**Fig III: Most commonly prescribed LMWH (N=200).**

In analysis of diagnosis where LMWH were prescribed includes, most prominent indication was Ischemic Heart Disease 75(37.5%), of the total prescriptions. This was followed by Stroke 26 (13%), Deep Vein Thrombosis 15 (7.5%), Cellulitis 9 (4.5%), Osteoarthritis 7 (3.5%) and others 36% (**Table.2**). In analysis of Coronary Syndromes (Non Q wave myocardial infarction and unstable angina), there was a remarkable increase in the percentage of LMWH prescription. LMWH has been evaluated in patients with acute coronary syndromes and in those undergoing percutaneous coronary interventions. This new class of anticoagulants has pharmacokinetic and biological advantages over UFH. These advantages have resulted in greater convenience afforded by the ability to administer LMWH by subcutaneous injection without laboratory monitoring, cost reductions from

reduced hospital stay. LMWHs especially Enoxaparin, Dalteparin and Ardeparin were approved by Food and Drug Administration of United States of America for their use in coronary syndrome.<sup>[1, 10, 11]</sup>

In analysis of Deep Vein Thrombosis, it was found that 7.5% of patients were given LMWHs for DVT. LMWHs were initially recommended for prophylaxis and treatment of DVT. These findings were similar to the study carried out by Michael. R. Lassen. et al<sup>[3]</sup> reduction in the risk of venous thrombosis with the use of reviparin during the period of immobilization is similar to the results of previous studies of patients receiving long-term prophylaxis after hip- or knee-replacement surgery. A recent meta-analysis documented similar reductions in symptomatic and asymptomatic venous thromboembolic events in patients who have undergone such surgery in a clinical trial of another low- molecular weight heparin in which compression ultrasonography was used to identify deep-vein thrombosis in immobilized patients, the incidence of asymptomatic deep vein thrombosis was reduced.<sup>[12, 13]</sup>

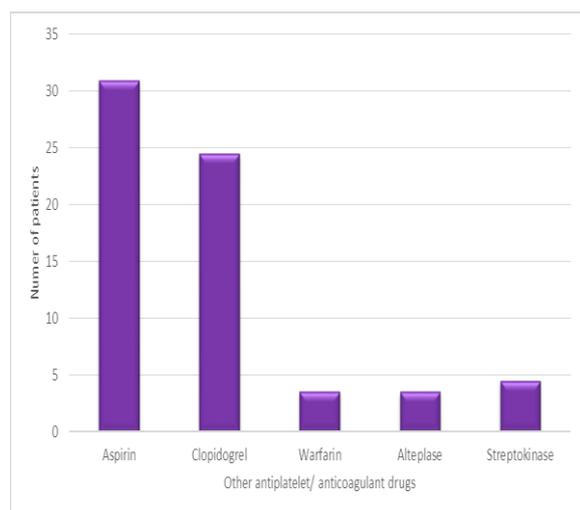
In analysis of Stroke, it was found that 13% of patients were given LMWHs in Stroke. Many recent studies and clinical trials are supporting the usage of LMWHs in Stroke. For patients with ischemic stroke treated within 48 hours of the onset of symptoms, these findings were similar to the study carried out by Richard. Kay, M.D.<sup>[14]</sup> In a meta-analysis of randomized trials of antithrombotic therapy in patients with ischemic stroke there was a significant, dose-dependent reduction in the risk of death or dependency at six months among the patients treated with Low molecular weight heparin. Main LMWH which is indicated for this therapy is Enoxaparin, Reviparin and Nadroparin.<sup>[14]</sup>

**Table II: Diagnosis wise distribution from the total population (n=200).**

DIAGNOSIS	NO. OF PATIENTS
IHD	75(37.5%)
Stroke	26 (13%)
DVT	15 (7.5%)
Cellulitis	9 (4.5%)
OA	7 (3.5%)
Hernia	7 (3.5%)
COPD	6(3%)
TIA	4 (2%)
Seizure	4 (2%)
Limb ischemia	3 (1.5%)
Left iliofemoral venous thrombosis	3 (1.5%)
Multi organ failure	3 (1.5%)
Foot ulcer	3 (1.5%)
Fracture	2 (1%)
Appendicitis	3(1.5%)
Left hemiparesis	2 (1%)
Left MCA infarct	2 (1%)
Post viral infection	2 (1%)
RHD	2 (1%)

RTA	2 (1%)
Respiratory failure	2 (1%)
Bowel obstruction	2 (1%)
Wound debriment	2 (1%)
ATT induced hepatitis	1 (0.5%)
Aorta iliac occlusion	1 (0.5%)
Adenomycosis	1 (0.5%)
Acute alcoholic pancreatitis	1 (0.5%)
Left SE incompetence	1 (0.5%)
Left SF incompetence	1 (0.5%)
Parieto temporal hemorrhage	1 (0.5%)
Pelvic obstruction	1 (0.5%)
Retroperitoneal tumor	1 (0.5%)
Renal cell carcinoma	1 (0.5%)
Kidney donor	1 (0.5%)
Hemiparesis	1 (0.5%)
Shoulder dislocation	1 (0.5%)
Spinal cord injury	1 (0.5%)
Polyarthritis	1 (0.5%)

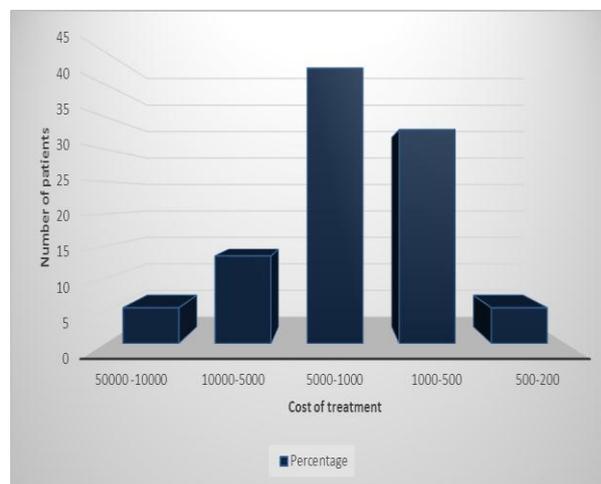
In analysis of other anticoagulant/antiplatelet drugs prescribed along with LMWHs, aspirin was prescribed for maximum number of patients 31% (n=62); this was followed by Clopidogrel 24.5% (n=49), Warfarin 3.5% (n=7), Alteplase 3.5% (n=7) and Streptokinase 4.5% (n=9) as illustrated in **fig 4**. For patients with acute STEMI whether or not they receive fibrinolytic therapy, it was recommend aspirin over no aspirin therapy at initial evaluation by health-care personnel followed by indefinite therapy. It was found that Aspirin constitutes the most prescribed antiplatelet drug along with LMWHs therapy. Aspirin decreases the incidence of rebound angina given along with heparin. For patients with acute STEMI, clopidogrel is recommended in addition to aspirin.<sup>[15]</sup>



**Figure IV: Analysis of antiplatelets / anticoagulants prescribed along with LMWH from the total population (n=200).**

In Cost analysis of different Low Molecular Weight Heparins, it was found that maximum number of patients was in 5000-1000 Rs range about 42.5% (N=85),

followed by 1000-500 Rs about 33% (N=66), 10,000-5000 Rs about 13.5% (N=27), 50,000-10,000 Rs about 5.5% (N=11), 500-200 about 5.5% (N=11) as illustrated in **fig 5**. This new class of anticoagulants has pharmacokinetic and biological advantages over UFH. These advantages have resulted in greater convenience afforded by the ability to administer LMWH by subcutaneous injection without laboratory monitoring, cost reductions from reduced hospital stay, a lower incidence of HIT and possibly a lower incidence of osteoporosis.<sup>[9]</sup>



**Figure V: Cost Analysis of Different Low Molecular Weight Heparins from the total population (n=200).**

Finally the study suggests the fact that the importance should be given always to the Low Molecular Weight Heparins than Unfractionated Heparins in antithrombotic therapy. Also continue education with regard to LMWHs is necessary to improve quality of these agents. Also implementation of guidelines for the use of LMWHs in total population would promote the rational use of LMWHs.

The benefits of LMWH therapy make it the currently emerging standard of care and cost effectiveness and convenience. The largest savings with LMWH result from a decrease in hospitalization time, hospital care comprises the greatest proportion of health care expenditures all over the world and methods of care which obviate the need for hospitalization lower the cost of health care.

### CONCLUSION

During the study period it was observed that the UFH prescription was only few when compared to LMWH. Hence it was found similar to various international guidelines principles of different countries. It was found that Low Molecular Weight Heparin prescriptions were increased for coronary syndromes, stroke and deep vein thrombosis etc. APTT monitoring was found to be inappropriate according to the LMWH prescribing guidelines. Also implementation of guidelines for the use of LMWHs in total population would promote the rational use of LMWHs. Thus, from the utilization evaluation, it was found that the prescription pattern of LMWHs was rationalized in the hospital.

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