



Low Molecular Weight Heparin (Enoxaparin) Induced Hematuria in covid-19 Patients, Experience at a Covid Dedicated Hospital

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Abstract

Introduction: The nightmare of Covid -19 is still not over, due to its antigenic diversity. Covid produces a hypercoagulable state and results in thrombosis which is one of the leading causes of death of Covid 19 patients. Low molecular weight heparin (LMWH)-enoxaparin has proven the benefit of reducing morbidity and mortality by reducing the thrombotic effect. But unfortunately, this anticoagulant can result haematuria and unnecessary hemorrhagic manifestation that may require immediate intervention. The exact scenario of enoxaparin-induced hematuria in the covid patient is still not explored by standard high-volume study.

Objective: Determine the incidence of hematuria by enoxaparin (LMWH) in covid-19 patients.

Material and method: The study was conducted over 210 cases for 6 months duration. Indoor patients receiving subcutaneous enoxaparin who tested positive for Covid19-RTPCR or who had signs of Covid in chest CT (Computerized Tomography) were enrolled. Both microscopic and gross haematuria cases were included in the current study.

Result: Out of 210 patients, only 5 patients (2.38%) developed haematuria. 2 had only microscopic and 3 had gross haematuria. Out of them, 3(60%) were male and 2(40%) were female. Hematuria was more common in those who received a higher dosage of enoxaparin.

Conclusion: This study found that enoxaparin-induced haematuria in the covid patient is not uncommon, and hematuria is significantly higher in patients receiving higher doses. Further high-volume study is recommended on this issue.

Keywords: Low molecular weight heparin (enoxaparin) microscopic and gross hematuria Covid-19

Introduction

Covid 19 has spread over the whole world. Repeated waves of covid 19 have become a nightmare for mankind. With ongoing research treatment of covid is updating regularly. To combat the hypercoagulable state of covid Low molecular weight heparin (LMWH)-enoxaparin is the treatment of choice.^{1,2} But due to its anticoagulant property, it results in unwanted hemorrhagic manifestation.²⁻⁵ Moreover, whether this

drug results significant haematuria is still ambiguous. It is necessary to detect the susceptible group who are at risk of haematuria that requires intervention. Intervention by titration of drug dose or withhold for a definite period regarding the risk and benefit is still unanswered.^{1,6,7} Any hemorrhagic manifestation should be recognized early and treated accordingly before resulting in morbidity or mortality. Otherwise, it may endanger life.

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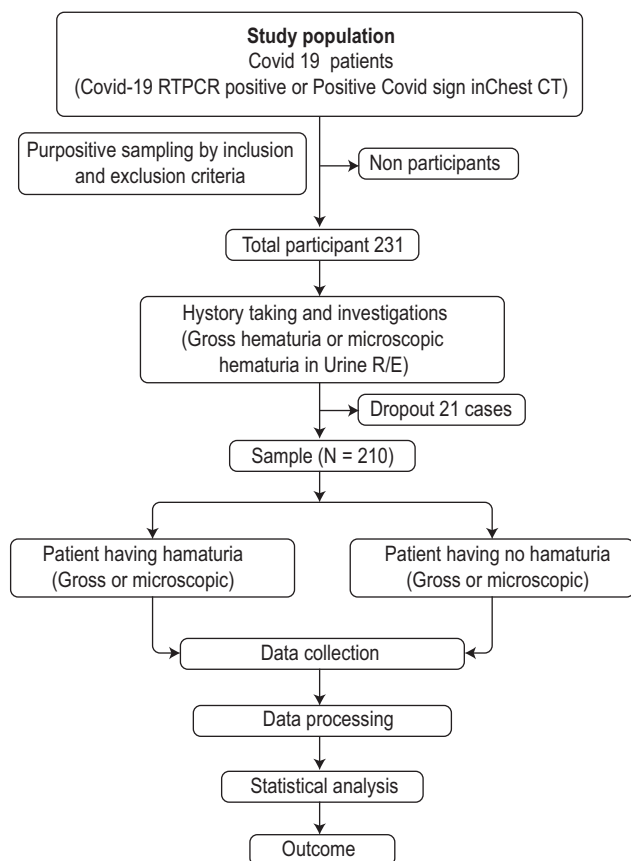
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So early prediction and treatment may be life-saving for the targeted group of patients. This study aimed to detect the impact of enoxaparin and resultant haematuria on covid 19 patients.

Materials and method:

It is an observational study, conducted in Covid dedicated Kurmitola General hospital (KGH), Dhaka, Bangladesh- for 6 months duration, from June 2021 to November 2021. Indoor patients having covid related symptoms and treated with subcutaneous LMWH (enoxaparin) were included. Either Covid 19 RTPCR positive or positive Covid signs in Chest CT (Computerized Tomography) were considered as the case. The sample size was 210. Patients with a history of preexisting hematuria, bleeding disorder, or pre-covid anticoagulant use, were excluded. Hematuria was documented by standard urine routine examination. By SPSS-23 data were analyzed, p vale < 0.05 was considered as significant.



Result

The total sample size was 210. Most (30.47%) were of the 40-49 age group (Table-I).

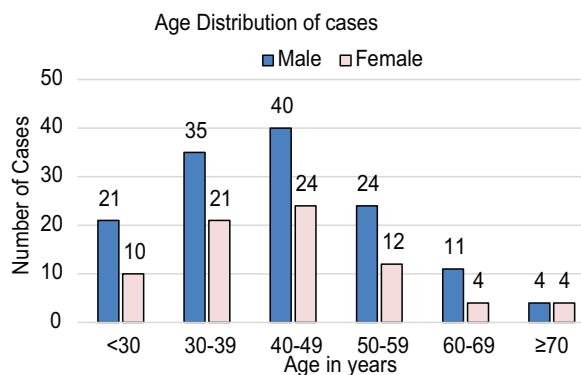


Fig.- 1: Age distribution of cases.

The minimum age was 10 and the maximum age was 80 years. The mean age was 42.62 years.

Out of 210 cases, 135 were male (64.28%) and 75 were female (35.72%) shown in table II.

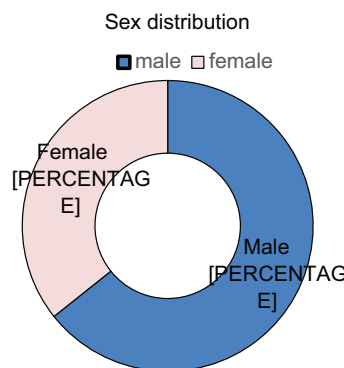


Fig.- 2: Sex Distribution of cases.

5(2.38%) cases had hematuria, 3 were male and 2 were female. Among these cases mean age for males was 33.7 years and females 34.6 years. (Table 3)

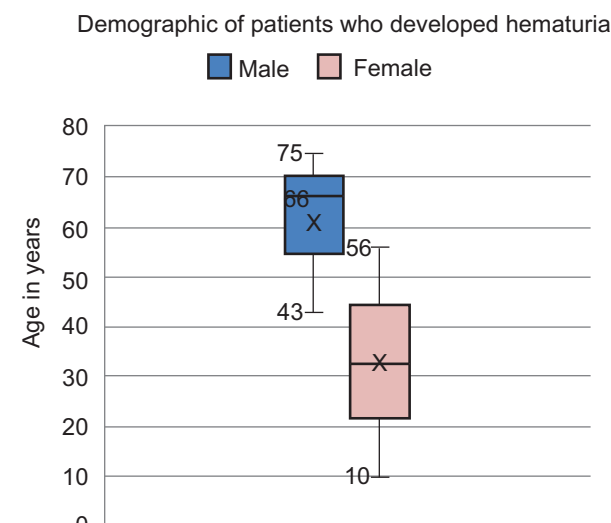


Fig.- 3: Demography of patients having hematuria.

The mean age for the male who developed hematuria was 61.33 years whereas the mean age of females having hematuria was 33 years (Fig.- 3).

Table 1: Relation of hematuria with the dose of enoxaparin.

Dose	Hematuria	No hematuria	P value
≤40mg daily	1	123	0.037619 ^s
>40 mg daily	4	82	

^s=significant, p-value obtained by Fisher Exact test

The relation between hematuria and the dose of enoxaparin was statistically significant (p-value 0.03), obtained by Fisher Exact test (Table 1).

Discussion:

Covid -19 produces a hypercoagulable state.⁸ Anticoagulant reduces the covid hypercoagulability-related morbidity and mortality.^{6,7,9}

In the current study, out of 210 patients, 135(64%) were male and 75 (36%) were females (Fig.-2). The mean age was 42.62 years. Most of the patients were of the 40-49 age group (Fig.-1). Only 5 patients (2.38%) developed haematuria. 2 had only microscopic and 3 had gross haematuria. 3(60%) were male and 2(40%) were female (Fig.-3). Among those 5 patients, 4 received a relatively higher dose of enoxaparin (>40 mg/day subcutaneous dose). Only one patient developed hematuria with a relatively lower dose of enoxaparin (≤40 mg/day subcutaneous dose). It was found that patients who received a higher dose of enoxaparin had significantly higher incidence of hematuria (p-value 0.03). (Table-1)

Another study found a higher incidence of clinically significant bleeding (6%) by high-dose enoxaparin in comparison to the current study (5). The mean age of the patient was relatively higher 66.2 years in that study. High therapeutic enoxaparin dose and inclusion of a greater number of critical cases may contribute to higher incidence of hemorrhage and hematuria. In the multivariant analysis of that study, age was a significant factor for bleeding, but the bleeding was not significantly related to sex, which supplements the current study result. This study found higher enoxaparin dose results in a higher incidence of hemorrhagic events which is supplemented by the study result of Musoke et al. Another study commented, even a low therapeutic dose of enoxaparin

may result in serious bleeding (2). Pre-existing comorbid factors, other ongoing medications may have the role for it. On other hand, many studies mentioned thrombotic effects with prophylactic (low dose) anticoagulants in Covid patients (10). So those studies recommended a higher dose of enoxaparin to combat the covid related thrombotic effects. Considering these factors, the risk of thrombosis and the benefits of the higher dose of enoxaparin should be judged critically before implication.

Conclusion:

This study concludes that enoxaparin-induced haematuria in the covid patient is low but not uncommon. Patients treated with a higher dose of enoxaparin had a higher incidence of hematuria. Further high-volume study is advocated on this concern.

Recommendation:

Incidence of Enoxaparin-induced hematuria is low, but high dose enoxaparin should be used with caution for treating the covid patients weighing the thrombotic risks and benefits.

Limitation:

It is single centered study. Moreover, the effect of associated co-morbidity, disease severity, other hematological parameters of Covid patients may alter the hematuria status, which is not explored in this study.

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