Frequency of Low Molecular Weight Heparin Indications among Sample of Pregnant Women in Salahadeen General Hospital, 2022

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Abstract

Background: Risk stratification for pregnant women to prevent venous thromboembolic events is routine in many high-income settings. Most healthcare professionals use the Royal College of Obstetricians and Gynaecologists Greentop guidelines for antenatal and postnatal risk assessment. Based on the score, women at high risk will receive thromboprophylaxis for varying lengths of time.

Aim: The current study aimed to find out the indications of low molecular weight use in pregnancy and the most common predictors of its use.

Patients and methods: A cross-sectional study was conducted in Salahadeen General Hospital /Gynecology and Obstetrics department during the period from the 1st of January to the 30th of June 2022. A convenience sample of 80 pregnant women attended the Gynecology and Obstetrics Department and reported LMWH use during the current pregnancy. Pregnant women who were unsure about the dose or the cause of LMWH use in their current pregnancy were excluded from the study.

Results: Recurrent abortion was the commonest indication of low molecular weight heparin use in the pregnancy as 15 (18.8%) of the participants had a recurrent abortion, followed by COVID-19 infection 13.8), and deep vein thrombosis in the last pregnancy (13.8%). While the least common indications were intrauterine growth retardation and in vitro fertilisation. The mean gestation age differed according to the indication of LMWH use. It was 17.6 (10.2) weeks in recurrent abortion, and 12.0 in the case of in vitro fertilisation.

In conclusion, the recurrent abortion of unknown cause, followed by COVID-19 infection, deep vein thrombosis in the last pregnancy, and hypertension were the commonest cause of low molecular weight heparin use during pregnancy. Although the drug is both safe and efficacious, its use for some indications has no proven scientific evidence.

Keywords: Heparin, Pregnancy, Salahadeen General Hospital.

DOI: 10.47750/pnr.2022.13.S03.192

INTRODUCTION

Normal pregnancy is accompanied by increased physiological changes (including increased concentrations of factors VII, VIII, and von Willebrand factor and by pronounced increases in fibrinogen), these changes make the pregnancy in a hypercoagulable state[(1)]. Accordingly, pregnancy increases the risk of thrombosis four- to five-fold, these changes may protect the pregnant women against the bleeding challenges of pregnancy, miscarriage, or childbirth[(2)]. The risk further increases if the pregnant women had other associated medical comorbidities, including genetic and acquired risk factors[(2, 3)].

The pro-coagulant state of pregnancy could contribute to the occurrence of gestational vascular complications (preeclampsia, placental abruption, fetal growth restriction, late and recurrent early miscarriage, intrauterine death, and stillbirth)[(4)].

Anticoagulation with low molecular weight heparins (LMWHs) is a well-established antithrombotic practice for primary and secondary thromboprophylaxis during pregnancy[(5)]. The advantages of LMWH over unfractionated heparin (UFH) include an enhanced anti-Xa to anti-IIa ratio

resulting in a more stable and predictable dose-response curve with no routine monitoring and reduced risk of bleeding, osteoporosis and heparin-induced thrombocytopenia[6].

There has been evidence that heparin and its derivatives could exert a beneficial effect in preventing gestational vascular complications(5). In the context of pregnancy, LMWH is used for prophylaxis and treatment of venous thromboembolism (VTE) and may be used to prevent systemic embolism in women with mechanical heart valves. LMWH is also administered for VTE prophylaxis in women with high-risk hereditary thrombophilia and has been prescribed in women with a previous history of adverse outcomes of pregnancy[6].

VTEs in those with infection COVID-19 are driven by strong activation of all aspects of Virchow's triad; patients are less mobile, have a prothrombotic state and the endothelium is activated. This may be exacerbated in pregnant women because of their prothrombotic background state and reduced flow in their leg veins[7]. Due to their anticoagulant properties, LMWH may be beneficial in patients with COVID-19 because of their anti-inflammatory properties, which include binding to inflammatory cytokines, inhibiting neutrophil chemotaxis and leukocyte migration, neutralizing the positively charged peptide complement factor C5a and sequestering acute phase proteins[8]. Risk stratification for pregnant women to prevent venous thromboembolic events is routine in many high-income settings. Most healthcare professionals use the Royal College of Obstetricians and Gynaecologists (RCOG) Greentop guidelines for antenatal and postnatal risk assessment. Based on the score, women at high risk will receive thromboprophylaxis for varying lengths of time[7]. The current study aimed to find out the indications of low molecular weight use in pregnancy and the most common predictors of its use.

PATIENTS AND METHOD

A cross-sectional study was conducted in Salahadeen General Hospital /Gynecology and Obstetrics department during the period from the 1st of January to the 30th of June 2022.

Ethical considerations

The study was proposed and subsequently approved by the scientific committee of the College of the Medicine/University of Tikrit. Fully informed consent was obtained from the patients verbally after explaining the aim of the study thoroughly and clearly with ensuring the anonymity and confidentiality of responses.

Sampling method and inclusion criteria

A convenience sample of 100 pregnant women attended the Gynecology and Obstetrics Department and reported LMWH use during the current pregnancy.

Exclusion criteria

Pregnant women who were unsure about the dose or the cause of LMWH use in their current pregnancy were excluded from the study.

Data collection

The researcher designed a standardized questionnaire after reviewing relevant literature and used it to retrieve the following information:

- Sociodemographic characteristics: Age, employment, residency.
- Obstetrical history: parity, gravidity, history of abortion, the complication of previous pregnancies, number of previous cesarean sections, and recurrent pregnancy losses.
- Medical history: Including chronic diseases including heart diseases, diabetes, hypertension, cancer, chronic respiratory diseases, chronic deep vein thrombosis, and thrombophilias).
- The indication(s) of LMWH use in the current pregnancy
- The dose and time of LMWH use.

RESULTS

A total of 80 pregnant women were enrolled in the current study, about 22.5 of them had an age of less than 20 years, while only two women (2.5%) had an age of ≥40, as shown in table 1.

Table 1: Sociodemographic distribution of the participants

Gender and Age		N	%
Age (years)	<20	18	22.5
	20-29	34	42.5
	30-39	26	32.5
	≥40	2	2.5
Residency	Rural	59	73.8
	Urban	21	26.3
Occupation	Housewife	53	66.3
	Employed	27	33.8
Educational level	Illiterate	15	18.8
	Primary school	28	35.0
	Secondary school	25	31.3
	College or higher	12	15.0

Regarding the obstetrical history, about 41.3% of the participants had 1-3 gravidity, more than half of them had no previous abortion, and 56.3% did not have a cesarean section, as shown in table 2.

Table 2: Obstetrical history of the participants

Gender and Age		N	%
Gravidity	1-3	33	41.3
	4-6	36	45.0
	≥7	11	13.8
Parity	≤3	57	71.3
	>3	23	28.7
Abortion	0	51	63.7
	1	10	12.5
	2	9	11.3
	3	7	8.8
	4	3	3.8
Cesarean section	0	45	56.3
	1	11	13.8
	2	11	13.8
	3	8	10.0
	4	5	6.3

Recurrent abortion was the commonest indication of LMWH use in the pregnancy as 15 (18.8%) of the participants had a recurrent abortion, followed by COVID-19 infection 13.8), and DVT in the last pregnancy (13.8%). While the least common indications were IUGR and in vitro fertilisation (IVF), as shown in table 3.

Table 3: Indication of the low molecular weight of heparin

	N	%
Recurrent abortions	15	18.8
COVID-19	11	13.8
Hypertension	11	13.8
DVT in last pregnancy	11	13.8
Systemic lupus erythematosus	9	11.3
Increased uterine artery resistance	8	10.0
Preeclampsia in last pregnancy	8	10.0
Twin	6	7.5
Thrombophilia	5	6.3
Elevated anti-cardiolipin	5	6.3
Diabetes	5	6.3
Obesity	5	6.3
Smoking	4	5.0
Heart disease	3	3.8
Varicose vein	3	3.8
Pulmonary embolism in the last pregnancy	2	2.2
Decreased amount of ligure	2	2.5
Intrauterine growth retardation	1	1.3
In vitro fertilisation	1	1.3

Some patients had more than one indication

The mean gestation age differed according to the indication of LMWH use. It was 17.6 (10.2) weeks in recurrent abortion, and 12.0 in the case of IVF, as shown in tabe 4.

Table 4: Gestational age according to the indications of low molecular weight heparin

Indications	Gestational age (weeks)
	Mean (SD)
Recurrent abortion	17.6 (10.2)
COVID-19	21.1 (9.8)
Hypertension	14.9 (10.9)
DVT in last pregnancy	13.0 (6.3)
Systemic lupus erythematosus	16.6 (9.8)
Increased uterine artery resistance	20.5 (8.7)
Preeclampsia in last pregnancy	16.5 (88)
Twin	24.6 (4.4)
Thrombophilia	19.8 (7.8)
Elevated anti-cardiolipin	12.6 (10.2)
Diabetes	16.2 (9.8)
Obesity	22.8 (8.6)
Smoking	15.0 (6.0)
Heart disease	8.0 (0.0)
Varicose vein	23.3 (9.8)
Pulmonary embolism in the last pregnancy	15.5 (6.3)
Decreased amount of ligure	30.0 (4.2)
Intrauterine growth retardation	28.0 (0.0)
In vitro fertilisation	12.0 (0.0)

The doses of LMWH ranged from one dose before the cesarean section as in some cases of hypertension and diabetes to 6000 IU according to the indication of its use, as shown in table 5.

Table 5: Dose of low molecular weight heparin used in the current study

Indications	N	Dose		
		2000	4000	6000
		N (%)	N (%)	N (%)
Recurrent abortion	15	0 (0.0)	14 (93.3)	1 (6.7)
COVID-19	11	2 (18.2)	6 (54.5)	3 (27.3)
Hypertension**	11	0 (0.0)	8 (72.7)	1 (9.1)
DVT in last pregnancy	11	0 (0.0)	7 (63.6)	4 (36.4)
Systemic lupus erythematosus	9	2 (22.2)	3 (33.3)	4 (44.4)
Increased uterine artery resistance	8	1 (12.5)	2 (25.0)	5 (62.5)
Preeclampsia in last pregnancy	8	0 (0.0)	7 (87.5)	1 (12.5)
Twin	6	0 (0.0)	3 (50.0)	3 (50.0)
Thrombophilia	5	0 (0.0)	2 (40.0)	3 (60.0)
Elevated anti-cardiolipin	5	0 (0.0)	4 (80.0)	1 (20.0)
Diabetes*	5	0 (0.0)	4 (80.0)	0 (0.0)
Obesity	5	0 (0.0)	4 (80.0)	1 (20.0)
Smoking	4	0 (0.0)	4 (100.0)	0 (0.0)
Heart disease	3	0 (0.0)	1 (33.3)	2 (66.7)
Varicose vein	3	0 (0.0)	3 (100.0)	0 (0.0)
Pulmonary embolism in the last pregnancy	2	0 (0.0)	0 (0.0)	2 (100.0)
Decreased amount of ligure	2	0 (0.0)	1 (50.0)	1 (50.0)
Intrauterine growth rtardation	1	0 (0.0)	1 (100.0)	0 (0.0)
In vitro fertilisation	1	0 (0.0)	1 (100.0)	0 (0.0)

Regarding the complications, 10% of the participants had an antepartum haemorrhage, 11.3% had a postpartum haemorrhage, and 5% needed blood transfusion (Table 6).

Table 6: Complications of low molecular weight heparin in pregnancy

Gender and Age	N	%
Antepartum haemorrhage	8	10.0
Postpartum haemorrhage	9	11.3
Blood transfusion	4	5.0

DISCUSSION

Systematic reviews suggest that LMWH therapy appears to be safe and efficacious when used in pregnant women. There is, however, poor consensus and a wide disparity of views among experts about the appropriate dose for the varying indications, the duration of treatment, and whether and how LMWH should be monitored because of the lack of an evidence base. These areas of uncertainty reflect the fact that clinical practice has grown largely through the publication of small observational studies and personal experiences[8].

In the current study, recurrent abortion was the most common indication of LMWH use in pregnancy, followed by COVID-19, hypertension, DVT in the last pregnancy, and systemic lupus erythematosus. In comparison, another study that was done in India in 2018 by Ankita et al. revealed that heart disease, chronic deep vein thrombosis, thrombophilias, and recurrent abortion were the commonest indication of LMWH use in pregnancy[9]. Another study done in India in 2013 reported that pregnant women with heart disease, DVT, thrombophilia, and recurrent abortion were the most common users of LMWH[10].

In the United States, Kominiarek et al revealed that a history of DVT, a history of pulmonary embolism, thrombophilia, and heart disease was the commonest indications[11]. Venous thromboembolism was the commonest indication of LMWH use in pregnancy in Greece as revealed in a study was done there in 2019[5].

The effectiveness of LMWH in preventing miscarriage or unexplained recurrent pregnancy loss remains controversial[12]. Fangfei et al. suggested that LMWH could improve live births and reduce the miscarriage rates of recurrent pregnancy loss. Therefore, LMWH might be a good treatment choice for women with unexplained recurrent pregnancy loss[13]. In Canada, a study was done there revealed that LMWH was the anticoagulant of choice in COVID-19 associated coagulopathy and was provided by 77% of respondents, with 60% using standard prophylactic dosing[14]. Regarding the complications, about ten percent of the patients had ante and postpartum haemorrhages. In comparison, the same results were obtained in another study that was done in the United States[13]. In Greece, a study was done there revealed that only 1.6 of pregnant women with LMWH use had bleeding during their pregnancy[15]. Women treated with LMWH had a higher risk of postpartum haemorrhage compared to controls but there was no difference in the mean of blood loss at delivery and risk of blood transfusion at delivery, respectively(6).

CONCLUSION

1. The recurrent abortion of unknown cause, followed by COVID-19 infection, DVT in the last pregnancy, and hypertension were the commonest cause of LMWH use during pregnancy.
2. Although the drug is both safe and efficacious, its use for some indications has no proven scientific evidence.

RECOMMENDATIONS

1. The prescription of LMWH during pregnancy must follow the updated guidelines with restrictions for pregnant women who need it.
2. Pregnant women with LMWH use must have close monitoring including both clinical and laboratory.

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