

To Assess the Outcome of Low Molecular Weight Heparin for Management of Females Presenting with Placental Insufficiency

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ABSTRACT

Introduction: Placental insufficiency is a serious condition that affects pregnant women and can lead to a range of complications during pregnancy. One potential treatment for this condition is the use of low molecular weight heparin.

Objectives: The main objective of the study is to assess the outcome of low molecular weight heparin for management of females presenting with placental insufficiency.

Material and methods: This descriptive case series was conducted in Unit II, Department of Obstetrics & Gynecology, Lady Willingdon Hospital, Lahore. Sample size of 175 cases was calculated with 95% confidence level, 4.5% margin of error and taking expected percentage of SGA i.e. 10.1% with LMWH in females placental insufficiency. Data was collected through non-probability consecutive sampling technique.

Results: In this present study total 175 females were enrolled. The mean age of the females was 29.70±6.36 years with minimum and maximum ages of 20 & 40 years respectively. In this study the mean gestational age of the females was 33.99±1.43 weeks with minimum and maximum values of 32 & 36 weeks respectively. 35(20%) females had null parity, 37(21.14%) females had primary, 45(25.71%) females had secondary parity and rest of the females belonged to multiple parity.

Practical implication: This study will be helpful in finding outcome by LMWH for management of females presenting with placental insufficiency

Conclusion: According to this study the outcome by LMWH for management of females presenting with placental insufficiency showed preterm delivery in 26.9% and SGA in 8% females.

Keywords: LMWH, Delivery, Patients, Pregnant, Treatment, Weight

INTRODUCTION

Placental insufficiency is a serious condition that affects pregnant women and can lead to a range of complications during pregnancy. One potential treatment for this condition is the use of low molecular weight heparin. However, the effectiveness of this treatment is still being debated by medical professionals. In this context, assessing the outcome of low molecular weight heparin for the management of females presenting with placental insufficiency is of great importance [1].

Placental insufficiency, also known as uteroplacental insufficiency, is a condition that occurs when the placenta is unable to provide the necessary nutrients and oxygen to the developing fetus. This can lead to a range of complications, including fetal growth restriction, preterm birth, and stillbirth. Placental insufficiency is a serious condition that requires prompt diagnosis and management to ensure the best possible outcome for both the mother and the baby [2]. Low molecular weight heparin (LMWH) is a type of anticoagulant medication that is commonly used to prevent blood clots in pregnant women who are at high risk for thromboembolic events³⁻⁵. In recent years, LMWH has also been used as a potential treatment for placental insufficiency, with some studies suggesting that it may improve fetal outcomes in affected pregnancies. Several studies have explored the use of LMWH for the management of placental insufficiency in females⁶. One such study, published in the Journal of Obstetrics and Gynaecology Canada, found that LMWH was associated with a significant reduction in the incidence of fetal growth restriction and preterm birth in women with placental insufficiency⁷. Another study, published in the Journal of Maternal-Fetal & Neonatal Medicine, found that LMWH improved fetal blood flow and oxygenation in pregnant women with placental insufficiency. Despite these promising findings, the use of LMWH for the management of placental insufficiency is still controversial. Some studies have failed to demonstrate a significant improvement in fetal outcomes with LMWH treatment, and there is concern about the potential risks associated with anticoagulant therapy during pregnancy⁸. Assessing the outcome of low molecular weight heparin for the management of females presenting with placental insufficiency is an important area of research. While some studies have suggested that LMWH may improve fetal outcomes in affected pregnancies, further research is needed to fully understand the potential benefits

and risks of this treatment. It is important for pregnant women with placental insufficiency to discuss all available treatment options with their healthcare provider to make an informed decision about their care⁹.

Objectives: The main objective of the study is to assess the outcome of low molecular weight heparin for management of females presenting with placental insufficiency.

MATERIAL AND METHODS

This descriptive case series was conducted in Unit II, Department of Obstetrics & Gynecology, Lady Willingdon Hospital, Lahore. Sample size of 175 cases was calculated with 95% confidence level, 4.5% margin of error and taking expected percentage of SGA i.e. 10.1% with LMWH in females placental insufficiency. Data was collected through non-probability consecutive sampling technique.

Inclusion criteria

- Females of age 20-40years, parity <5 with placental insufficiency (as per operational definition) presenting >30 weeks of gestation (on LMP).

Exclusion criteria

- Females with abnormal bleeding and clotting profile (PT>20sec, aPTT>15sec, INR>2)
- Females with thrombophilia (on medical record)
- Females with hypertension (BP≥140/90mmHg), gestational or chronic diabetes (BSR>186mg/dl), deranged LFT (ALT>40IU, AST>40IU), creatinine>1.2mg/dl.^{17,18}

Data Collection: 175 females fulfilling selection criteria were included through OPD of Department of Obstetrics & Gynecology, Lady Willingdon Hospital, and Lahore. Informed consent was obtained before including females in the study. Demographic profile (name, age, parity, gestational age) was noted. Then females were given Enoxaparin 40 mg intravenous. Then patients were followed-up there till delivery. If delivery was occurring before completion of 38 weeks, then preterm delivery was labeled (as per operational definition). After delivery, weight of baby was noted and if <10th percentile was labeled (as per operational definition). All this information was recorded on proforma.

Statistical Analysis: The collected data was entered and analyzed statistically by using SPSS version 20. Quantitative variables like age, gestational age, AFI and BMI was presented in

form of mean ± S.D. Qualitative variables like preterm delivery and SGA was presented in form of frequency and percentages. Frequency was calculated for parity. Data was stratified for age, gestational age, parity and BMI. Stratified group was compared by using chi-square test taking p-value<0.05 as significant.

RESULTS

In this present study total 175 females were enrolled. The mean age of the females was 29.70±6.36 years with minimum and maximum ages of 20 & 40 years respectively. In this study the mean gestational age of the females was 33.99±1.43 weeks with minimum and maximum values of 32 & 36 weeks respectively. 35(20%) females had null parity, 37(21.14%) females had primary, 45(25.71%) females had secondary parity and rest of the females belonged to multiple parity. Mean BMI of the females was 24.52±3.04 kg/m² with minimum and maximum values of 19.3 & 29.7 kg/m² respectively. According to this study the preterm delivery in females presenting with placental insufficiency were 47(26.9%).

Table 1: Descriptive statistics of patients

Variable	n	Mean	SD	Minimum	Maximum
Age (years)	175	29.70	6.36	20	40
Gestational age (weeks)	175	33.99	1.43	32	36
BMI (kg/m ²)	175	24.52	3.04	19.3	29.7

Table 2: Frequency distribution of preterm delivery

	Frequency		Percent
	Yes	No	
	Preterm delivery	47	
	Total	175	100.0

Females with age ≤ 30 years were 96 in which preterm delivery was found in 28 females, >30 years females were 79 in which preterm delivery was noted in 19 females, (p-value=0.447). The females with gestational age 32-34 weeks were 105 in which preterm delivery found in 47 females, (p-value=0.001*). The primary parity females were 72 in which preterm delivery found in 23 females, multiparity females were 103 in which preterm delivery found in 24 females, (p-value=0.204). Similarly females with normal BMI were 96 in which preterm delivery noted in 26 females, and the females with abnormal BMI were 79 in which preterm delivery noted in 21 females, (p-value=0.941).

Table 3: Comparison of age, gestational age, parity, BMI with preterm delivery of the females

	Preterm delivery		Total	p-value
	Yes	No		
Age (years)	≤ 30	28	68	0.447
	> 30	19	60	
Gestational age (weeks)	32-34	47	58	0.001
	35-36	0	70	
Parity	Primary	23	49	0.204
	Multiple	24	79	
BMI	Normal	26	70	0.941
	Abnormal	21	58	

Females with age ≤ 30 years were 96 in which females presented with SGA were 06, >30 years females were 79 in which females presented with SGA were 08, (p-value=0.347). The females with gestational age 32-34 weeks were 105 in which females presented with SGA were 14, (p-value=0.001*). The primary parity females were 72 in which females presented with SGA were 03, multiparity females were 103 in which females presented with SGA were 11 (p-value=0.159). Similarly females with normal BMI were 96 in which females presented with SGA were 06 and the females with abnormal BMI were 79 in which females presented with SGA were 08, (p-value=0.347).

Table 4: Comparison of age, gestational age, parity, BMI with SGA of the females

	SGA		Total	p-value
	Yes	No		
Age (years)	≤ 30	6	90	0.347
	> 30	8	71	
Gestational age (weeks)	32-34	14	91	0.001
	35-36	0	70	
Parity	Primary	3	69	0.159
	Multiple	11	92	
BMI	Normal	6	90	0.347
	Abnormal	8	71	

DISCUSSION

This present descriptive case series study was carried out at Unit II, Department of Obstetrics & Gynecology, Lady Willingdon Hospital, Lahore to assess the outcome of LMWH for management of females presenting with placental insufficiency. Several adverse obstetric outcomes such as pre-eclampsia, fetal growth restriction (FGR), placental abruption and stillbirth are associated with placental insufficiency¹⁰. LMWH may have favorable effects through pathways that have nothing to do with anti-coagulation. Heparins may influence trophoblast growth and development by decreasing apoptosis, serving as an indirect growth factor and decreasing inflammation via anti-complement and cytokine effects¹¹⁻¹². In this study due to LMWH for management of females presenting with placental insufficiency preterm delivery was found in 47(26.9%) females. The females presenting with placental insufficiency with SGA were 14(8%). Gestational age showed significant difference with preterm birth and females presented with small gestational age i.e. p-value=0.001¹³. Age, parity, BMI showed statistically insignificant effect with preterm delivery and small gestational age. Some of the studies are discussed below showing their results as. A study by Naheed Akhtar and Nazli Hameed documented that LMWH has definitive role in patients with adverse pregnancy outcome due to IUGR and oligohydramnios in the absence of APS and thrombophilias¹⁴. In a study, it was noticed that preterm delivery was 32.1% and SGA was 10.1% with LMWH in females presenting with placental insufficiency. O. Tica S. Dobre et al concluded that LMWH improve the pregnancy outcome in women with high risk of IUGR. The pregnancy ultrasound evaluation was considered essential for detecting the cases with placental mediated complications and for decreasing the risk of IUFD by indicating the optimal time for delivery in early-onset IUGR¹⁵. LMWH may act by improving placental development as well as by inhibiting reactive pathways involved in Pre-eclampsia and SGA. Hence, LMWH improved uteroplacental blood flow and thus improving perinatal outcome. Another study by Isma N et al concluded that treatment with a prophylactic dose of LMWH (dalteparin) during pregnancy was related to fewer women with prolonged first stage of labour, but also to an increased risk of prematurity and blood loss complications¹⁶.

CONCLUSION

According to this study the outcome by LMWH for management of females presenting with placental insufficiency showed preterm delivery in 26.9% and SGA in 8% females.

REFERENCES

- Rodger MA, Carrier M, Le Gal G, Martinelli I, Perna A, Rey E, et al. Meta analysis of low-molecular-weight heparin to prevent recurrent placenta-mediated pregnancy complications. *Blood* 2014;123:822-8.
- Simonazzi G, Curti A, Cattani L, Rizzo N, Pilu G. Outcome of severe placental insufficiency with abnormal umbilical artery Doppler prior to fetal viability. *BJOG* 2013;120(6):754-7.
- Krishna U, Bhalerao S. Placental Insufficiency and Fetal Growth Restriction. *J Obstet Gynaecol India* 2011;61(5):505-11.
- Akhtar N, Hameed N. Role of low molecular weight heparin in adverse obstetrical outcome in-patients due to oligohydramnios and severe IUGR. *Pak J Physiol* 2015;11(1):17-9.

5. Meekins J, Pijnenborg R, Hanssens M, McFadyen I, Asshe Av. A study of placental bed spiral arteries and trophoblast invasion in normal and severe pre-eclamptic pregnancies. *BJOG: An International Journal of Obstetrics & Gynaecology* 1994;101(8):669-74.
6. Boron WF, Boulpaep EL. *Medical Physiology, 2e Updated Edition E-Book: with STUDENT CONSULT Online Access: Elsevier Health Sciences*; 2012.
7. Gabbe SG, Niebyl JR, Simpson JL, Landon MB, Galan HL, Jauniaux ER, et al. *Obstetrics: normal and problem pregnancies e- book: Elsevier Health Sciences*; 2016.
8. Greenough A, Nicolaides KH, Lagercrantz H. Human fetal sympathoadrenal responsiveness. *Early human development* 1990;23(1):9-13.
9. Baschat AA, Gembruch U, Reiss I, Gortner L, Harman CR. Neonatal nucleated red blood cell count and postpartum complications in growth restricted fetuses. *Journal of perinatal medicine* 2003;31(4):323-9.
10. Thilaganathan B, Plachouras N, Makrydimas G, Nicolaides K. Fetal immunodeficiency: A consequence of placental insufficiency. *International Journal of Gynecology & Obstetrics* 1994;46(3):357-8.
11. Trudinger BJ, Cook CM, Thompson RS, Giles WB, Connelly A. Low-dose aspirin therapy improves fetal weight in umbilical placental insufficiency. *American journal of obstetrics and gynecology* 1988;159(3):681-5.
12. Miao Z, Chen M, Wu H, Ding H, Shi Z. Comparative proteomic profile of the human placenta in normal and fetal growth restriction subjects. *Cellular Physiology and Biochemistry* 2014;34(5):1701-10.
13. Say L, Gülmezoglu AM, Hofmeyr GJ. Bed rest in hospital for suspected impaired fetal growth. *The Cochrane Library* 1996.
14. Ramakrishnan U, Stein AD, Parra-Cabrera S, Wang M, Imhoff-Kunsch B, Juárez-Márquez S, et al. Effects of docosahexaenoic acid supplementation during pregnancy on gestational age and size at birth: randomized, double-blind, placebo-controlled trial in Mexico. *Food and nutrition bulletin* 2010;31(2_suppl2):S108-S16.
15. Neri I, Mazza V, Galassi MC, Volpe A, Facchinetti F. Effects of L-arginine on utero-placental circulation in growth-retarded fetuses. *Acta obstetrica et gynecologica Scandinavica* 1996;75(3):208-12.
16. Maharaj CH, O'Toole D, Lynch T, Carney J, Jarman J, Higgins BD, et al. Effects and mechanisms of action of sildenafil citrate in human chorionic arteries. *Reproductive Biology and Endocrinology* 2009;7(1):34.
17. Farid G, Warraich NF, Iftikhar S. Digital information security management policy in academic libraries: A systematic review (2010–2022). *Journal of Information Science*. 2023:01655515231160026.
18. Khalid A, Malik GF, Mahmood K. Sustainable development challenges in libraries: A systematic literature review (2000–2020). *The Journal of academic librarianship*. 2021 May 1;47(3):102347.