



# ORIGINAL RESEARCH PAPER

Obstetrics & Gynaecology

## HEPARIN INDUCED THROMBOCYTOPENIA IN AN ANTENATAL PATIENT WITH ATRIAL FIBRILLATION – CASE REPORT

KEY WORDS:

|                                 |   |
|---------------------------------|---|
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### BACKGROUND

Pregnancy is accompanied by various physiological changes of cardiovascular system in normal woman which predisposes them to arrhythmogenesis.

Rheumatic mitral valve disease is most common cause of atrial fibrillation(AF) during pregnancy which remains still endemic in developing countries.<sup>(1)</sup>Early detection and initiation of treatment with rate controlling drugs and anticoagulants can reduce the rise of thromboembolic events.

Unfractionated heparin &LMWH are the anticoagulant of choice in pregnancy for prevention & treatment of venous thromboembolic disease.

Heparin Induced Thrombocytopenia (HIT )is a rare but serious complication with heparin therapy raising thromboembolic event paradoxically.

Here we present a case of Atrial fibrillation in antenatal patient who developed heparin induced thrombocytopenia, who was successfully treated with injection fondaparinaux .

### INTRODUCTION

Pregnancy is accompanied by various physiological changes of cardiovascular system in normal women. Increase in estrogen level during pregnancy increase sensitivity to adrenergic receptors. Also increase in blood volume and cardiac output results in stretching of myocardium and increase in end diastolic volumes. There is also alteration in myocardial refractoriness due to augmented sinus heart rate.All this physiological changes predisposes pregnant women to arrhythmogenesis.<sup>(1)</sup>

Atrial fibrillation which is one of the most common cardiac arrhythmia affecting approximately 0.5-1% of total population is still rare in pregnancy and usually present as palpitation,dizziness and even syncope.Atrial fibrillation is associated with increase mortality (or 13.13,95% ci:7,77-22,21,p<0.0001) <sup>(3)</sup>hence management of atrial fibrillation includes rate control which is started at time of diagnosis and initiation of anticoagulant<sup>(2)(4)</sup>. The anticoagulant preferred for atrial fibrillation in pregnancy are heparin compounds .

Both LMWH & UFH are considered safe during pregnancy as neither of them cross placenta.<sup>(5)(6)</sup>

LMWH due to its better safety profile and fewer side effects like bleeding,thrombocytopenia and osteoporosis is preferred over UFH which needs multiple injections per day & monitoring with Aptt .

Heparin induced thrombocytopenia is a rare complication occurring in 0.3-3% of antenatal patients but is a serious complication due to increased thromboembolic events in 50% of untreated patients.<sup>(7)</sup>

Due to either lack of clinical evidence or contraindication to alternative therapeutic agents during pregnancy ,HIT stands out as a dilemma.

### Case Report

Presenting case of 33 year old female G4A3 with 34 week period of gestation with diagnosis of rheumatic heart disease and Atrial fibrillation since 14 weeks Period of gestation (pog).Patient gives history of palpitation at 14 week pog with persistent tachycardia for which 2D echo was done and diagnosed as RHD (moderate MS and MR with moderate TR with pulmonary hypertension) with Atrial fibrillation for which she was started on T.Lasix 20 mg OD, T.ACITROM 2mg OD, Inj.Enoxaparin 40 mg subcutaneous every 3 days , Inj .Penidure 1.5 lakh units every 21 days and T.Diltiazem 30 mg TID. On admission routine investigation (CBC, coagulation profile) was sent & Scan done showed fetal growth restriction (FGR ) (EFW <2 Percentile). Cardiologist opinion taken and was started on T.lasix 10 mg OD,T.metoprolol 25 mg OD ,Inj Penidure 12 LA once in 21 days and enoxaparin (LMWH) was converted to Unfractionated heparin 5000 U (with plan of termination of pregnancy if FGR was associated with Doppler changes in subsequent scans). Biweekly AFI with Doppler and platelet monitoring done every 2 days.At 36 week POG, Platelet count was 72000 ( reduced by > 50% from baseline platelet count of 220000 within 15 days of initiation of UFH). Cardiologist opinion was taken, heparin discontinued and was advised to start inj. Fondaparinaux .NST done on same day, was nonreactive hence patient was taken for emergency LSCS in view of FGR with a non reactive NST.A single life male baby of weight 1.8 kilogram was delivered.Inj.fondaparinaux was started after 12 hours post operatively and platelet was monitor every 2 days. There was improvement in platelet count from 72000 (POD0) to 92000 (Pod 2) to 1.02 lakh (pod5). Hence injection fondaparinaux was stopped and oral anticoagulant ( T.Acitrom 2mg OD) was initiated. Post operative period was uneventful and patient was discharged on Pod10 with T. ACITROM 2mg OD,T.LASIX 20 MG OD ,T.METXL 25 MG OD & INJ. Penidure 12 LA once in 21 days.

### DISCUSSION

Heparin which is commonly used for thromboprophylaxis or treatment of various clinical conditions including AF is associated with a rare but severe complication called Heparin induced thrombocytopenia (HIT)<sup>(8)(9)(10)(11)(12)</sup>

There are 2 different forms of HIT-HIT type I, HIT type II HIT type I ( non immune heparin associated thrombocytopenia) is a non immunological response due to direct interaction between heparin and platelets causing platelet clumping which develops within 48-72 hours of starting heparin treatment, which is characterized by transient or mild thrombocytopenia (plt< 100000/cu.mm), that returns to normal within 4 days once heparin is withdrawn. The diagnosis of HIT type-1 doesn't require any laboratory tests and is not associated with significant risk of thrombosis.<sup>(13)</sup>

HIT type II is immune mediated, which occurs due to antibody formation against the complex heparin/platelet factor 4(PF4) which then acts on FcR II a leading to activation of endothelium & platelets causing thromboembolic events.<sup>(14)(15)(16)</sup>

Diagnosis of HIT is based on 4T score which includes both clinical observation & laboratory analysis.<sup>(17)</sup>

4T Score estimates the incidence probability of developing HIT based on severity of thrombocytopenia, occurrence of thrombosis & time elapsed since receiving heparin therapy.

**Table1: Estimating the pre-test probability of heparin induced thrombocytopenia: the 4T's:**

| Category                         | 2 points   | 1 point   | 0 point                                  |
|----------------------------------|--|---|--|
| Thrombocytopenia                 | >50% fall, or nadir of 20-100×10 <sup>9</sup> /l                                 | 30-50% fall, or nadir of 10-19 10 <sup>9</sup> /l   | 3p% fall or nadir <10×10 <sup>9</sup> /l |
| Timing of platelet count fall    | Days 5 to 10, or ≤1 day of heparin exposure within past 30 days                  | >Day 10 or unclear (but fits with HIT), or ≤1 day if heparin exposure within past 30-100 days | ≤ 1 day (no recent heparin)              |
| Thrombosis or other sequelae     | Proven thrombosis, skin necrosis or after heparin bolus, acute systemic reaction | Progressive, recurrent or silent thrombosis; erythematous skin lesions                        | None                                     |
| Other cause for thrombocytopenia | None evident   | Possible  | Definite                                 |

Gradual drop of platelets (5-10 days of receiving heparin 30 days of heparin therapy) either during hospitalisation or after discharge in patients with heparin therapy should fortify the clinical suspicion of HIT.

Eventhough HIT is associated with thrombocytopenia ,alternative anticoagulant which has effective antithrombotic activity is strongly recommended.<sup>(18)</sup>

Alternative anticoagulants used during pregnancy include danaparoid, argatroban, fondaparinux.

Danaparoid has shown promising outcome in treatment of heparin induced thrombocytopenia but due to its non availability in developing countries it is less commonly used whereas Argatroban lacks human data regarding their use in pregnancy.<sup>(19)(20)</sup> Fondaparinux which is a direct thrombin inhibitor has proven to be effective anticoagulant in most of the studies and also has advantage of once daily subcutaneous administration and does not require laboratory monitoring hence Fondaparinux is preferred for this case which showed promising result.<sup>(21)(22)</sup>

## CONCLUSION

Heparin induced thrombocytopenia is a serious complication associated with heparin therapy diagnosed based on clinical suspicion, 4Tscore. It's management include immediate discontinuation of heparin and switch over to alternative anticoagulant. A multidisciplinary approach will always prove to be worth to make appropriate clinical decision and reduce the thromboembolic event in turn reducing mortality.

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