Oral Anticoagulation Dose and Risk of Postpartum Bleeding Complications after Cesarean Section in Patients with Mechanical Heart Valve Prosthesis

Maged Ahmed Abdel Raouf[1], Amir Araby Gabr[2], Tarek El Husseiny Mohamed[3], Amr Samir Fouad Tammam[4*], Ghada Youssef[5]

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Abstract

Background: Patients with mechanical heart valves have an elevated risk of maternal morbidity and mortality after delivery. This work aimed to compare the occurrence of postpartum bleeding complication in relation to warfarin dose after cesarean delivery in cases with mechanical heart valve prosthesis.

Methods: This cross-sectional research involved 57 high risk pregnancy outpatient clinics of 20-40 years old and had mechanical prosthetic mitral and/or aortic valves. All patients underwent thorough history taking, general examination, preoperative routine laboratory investigations (coagulation profile, liver & kidney functions, complete blood count, and fasting & 2h postprandial blood glucose levels) and antenatal ultrasonography.

Results: 1ry postpartum haemorrhage was found in one patient, intraperitoneal haemorrhage was found in two patients, SC hematoma was found in 3 patients, and SR hematoma was found in 3 patients. While no cases of valve thrombosis or other thromboembolic events were reported. SC hematoma started with mean of 14.45 cm^2 and reached 8.43 cm^2 on day 14. While SR hematoma started with mean of 33.04 cm^2 and reached 11.81 cm^2 on day 14. Mean of biggest hematoma size recorded was 6.1 cm and ranged from 3 – 10.

Conclusions: Women with prosthetic heart valves who are of childbearing age should be counselled about potential pregnancy complications. The incidence of 1ry postpartum hemorrhage in individuals receiving Warfarin is roughly 1.8%; according to the existing data, Warfarin is the optimal choice for patients with prosthetic heart valves during pregnancy.

Keywords: Oral Anticoagulation; Postpartum Bleeding; Complications; Cesarean Section; Mechanical Heart Valve Prosthesis

[1] Professor of Obstetrics and Gynecology, Faculty of Medicine, Cairo University, Egypt.
[2] Assistant Professor of Obstetrics and Gynecology, Faculty of Medicine, Cairo University, Egypt.
[3] Lecturer of Obstetrics and Gynecology, Faculty of Medicine, Cairo University, Egypt.
[4] Assistant lecturer of Obstetrics and Gynecology, Faculty of Medicine, Cairo University, Egypt.
[5] Assistant Professor of Cardiovascular Medicine, Faculty of Medicine, Cairo University, Egypt.
[*]**Corresponding Email:** amr4thsamirdr.001@gmail.com

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Introduction

Pregnancy poses a set of unique challenges for women with mechanical prosthetic valves. With mechanical prosthetic valves, the incidence of thromboembolic events increases during pregnancy [1]. There is an increase in stroke volume, heart rate & hemodynamic load during pregnancy. Additionally, there is a 30 - 40 % increase in the cardiac output accompanied by a drop in total peripheral resistance that results in a reduction in blood pressure [2].

The rise in maternal hormones and circulating procoagulant substances results in a reduction in thrombin time, prothrombin time, activated partial thromboplastin time & INR [3]. In pregnant women with prosthetic mechanical valves, thromboembolism rates ranged from 7 - 23 % per patient per year[4, 5].

Despite recommendations that VKA should be the first-line antepartum therapy, low-molecular-weight heparin (LMWH) is a significantly less effective anticoagulant, and various research indicate that the risk of embryopathy is low roughly 1 - 2 % when the mother is on warfarin at 5 mg per day or less [6]. Recent recommendations classify warfarin as class I during the 2nd& 3rd trimesters, as the warfarin embryopathy risk is limited to weeks 6 to 12. During the 1st trimester, warfarin doses of 5 mg/day or less are categorized

as class IIa, making it superior to unfractionated or LMWH [7, 8].

Patients with mechanical heart valves have an elevated risk of maternal morbidity and mortality after delivery. Morbidity consists of intra-abdominal bleeding, wound hematoma, primary and subsequent postpartum hemorrhage, the necessity for reoperation or another approach, valve thrombosis, and other thromboembolic symptoms as stroke. Although, there are few recommendations on when oral anticoagulants should be initiated in the postpartum period[9].

To minimize competing hazards, sequelae of valve thrombosis and obstetrical bleeding, and thus to maximize maternal outcomes and produce evidence-based guidelines for postpartum anticoagulation therapy, pooled institutional data and an interdisciplinary approach are advocated [10].

The objective of this research was to assess the incidence of postpartum bleeding complications in relation to warfarin dosage following cesarean delivery in patients with mechanical heart valve prosthesis.

Patients and Methods

This cross-sectional researchinvolved 57 high risk pregnancy outpatient clinics of 20-40 years old and had mechanical prosthetic mitral and/or aortic valves due to rheumatic heart disease admitted to Kasr Al Ainy high risk pregnancy outpatient clinic.

An informed written consent was obtained from the patient or relatives of the patients. The study was done after approval from the Ethical Committeeof Kasr Al Ainy Hospital (approval code:).

Patients declined to participate, those with hypertensive disorders, history of any thrombotic events, right sided mechanical heart valves, with known bleeding or coagulation disorders, known thrombophilia and diabetic patients were excluded.

All cases subjected to full history taking involving age, history of any medical disorder, parity, gestational age on admission, duration since cardiac surgery, type, number & location of replaced cardiac valves, average warfarin therapeutic dose utilized during pregnancy, type & dose of anticoagulant immediately used before delivery, history of prosthetic valve or obstetric complications.General examinationinvolving maternal height &weight and obstetric examination was performed.

Preoperative routine laboratory investigations:

Coagulation profile (to ensure that the INR is <1.5 &PC is >60% the prior to surgery), complete blood count, kidney &liver functions, and fasting and 2 h postprandial blood glucose levels.

Antenatal ultrasonography:

It was performed to assess the gestational age and to evaluate the fetal health. Afterwards, a Cardiology consultant examined all patients to evaluate the cardiac status, determine the anticoagulation dose, monitor the occurrence of cardiac complications, and assist in determining the time and method of termination based on the circumstances of the individual patient.

Participants were followed up starting from 36 weeks of gestation (or earlier if there are risks of preterm delivery e.g., preterm contractions), warfarin was stopped, and adjusted therapeutic doses of unfractionated heparin were provided to patients in order to keep the activated partial thromboplastin time (aPTT) within the therapeutic range (i.e.,to maintain a mid-interval aPTT between 2 - 2.5 times the patient's baseline value).The administration of unfractionated heparin was discontinued 6 hrs. prior to the scheduled elective caesarean surgery that was performed by the same skilled surgical group.

The amount of blood in the sub-rectus and intraperitoneal drains was documented if a patient experienced bleeding issues. To check for symptoms of intraperitoneal hemorrhage or wound hematoma, transabdominal ultrasonography & clinical examination were performed daily until the end of the hospital stay, then 1 and 2 weeks later.

The ultrasonographic results indicating the existence of an intraperitoneal haemorrhage or hematoma or subcutaneous sub-rectus hematoma included the presence of a homogenous or heterogeneous fluid collection within the peritoneal cavity or the abdominal walland Doppler color flow did not consistently detect the existence of active extravasation; hence, the size of the hematoma was measured in centimetres and daily monitoring was performed. Using these ultrasonographic criteria, hematomas were identified.

The primary outcome was occurrence of sub-rectus and /or subcutaneous hematoma, intra-abdominal bleeding, required packed RBCs transfusion, required wound hematoma evacuation or abdominal re-exploration, need for any other approach and occurrence of valve thrombosis or other thromboembolic manifestations. Thesecondary outcomes were hospital stay and need for blood transfusion will be assessed.

Statistical analysis

Statistical analysis was done by SPSS v28 (IBM Inc., Chicago, IL, USA). Qualitative data were presented as frequency and percentage (%). Quantitative data were presented as mean (±SD).

Results

Table 1 shows that mean age was 32.33 ± 5.1 years with mean BMI of 31.33 ± 3.05 kg/m2. Meanwhile, mean gravidity was 2.09 ± 1.74 and mean parity 1.51 ± 1.29 with mean GA at delivery was 38.27 ± 0.651 weeks. 3.6% of the patients had

history of SR hematoma, 3.6% had history of recurrent abortion, and 7.3% had history of IUGR.

Table 1: Basic characteristics among studied patients

Variable	Mean ± SD	Range
Age (years)	32.33 ± 5.1	20 - 40
Weight (kg)	80.96 ± 9.76	68 – 105
Height (cm)	160.67 ± 5.61	145 – 178
BMI (kg/m^2)	31.33 ± 3.05	26.35 – 39.1
Gravidity	2.09 ± 1.74	0 - 8
Parity	1.51 ± 1.29	0 - 4
Previous CS	1.4 ± 1.26	0 - 4
Living offspring	1.49 ± 1.26	0 - 4
GA on delivery (weeks)	38.27 ± 0.651	37 - 40
Associated medical conditions,	N	%
Bronchial asthma	1	1.8%
HCV	1	1.8%
History of obstetric complications,		
S.R hematoma	2	3.6%
Recurrent abortion	2	3.6%
IUGR	4	7.3%

BMI: Body mass index, CS: cesarian section, GA: gestational age, HCV: hepatitis C virus, IUGR: Intrauterine growth restriction

The indication of CS was breech in 3(5.5%) patients, CPD in 10 (18.2%) patients, IUGR n 1 (1.8%) patients and repeated CS in 41 (74.5%) patients. **Table 2, Figure 1**

Table 2: Indication of CS distribution among studied patients

Variable	N	%
Breech	3	5.5%
CPD	10	18.2%
IUGR	1	1.8%
Repeated CS	41	74.5%

CPD: cephalopelvic disproportion, CS: cesarian section, IUGR: Intrauterine growth restriction

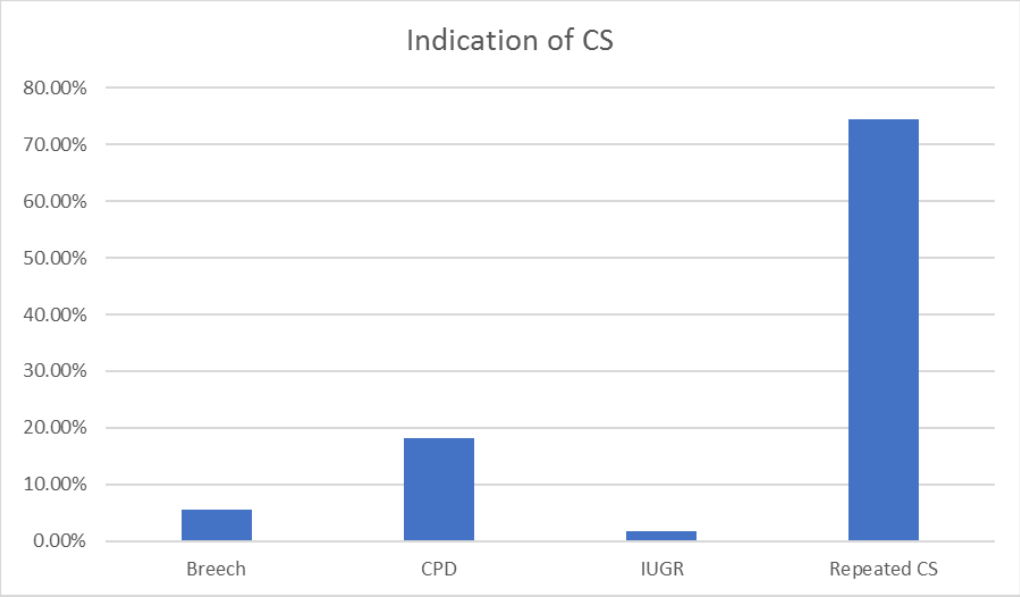

Figure 1: Indication of CS distribution among studied patients

Table 3 shows that 81.9% of the patients had one valve replaced, and 18.2% of the patients had two valves replaced. 54.5% of the patients had mitral replaced, 27.3% had aortic replaced, and 18.2% had both mitral and aortic replaced. Mean Warfarin dose during pregnancy was 6.58 mg and mean Total daily dose of heparin was

32818 IU. Moreover, mean total blood loss was 812.55 ml and amount of blood transfused was 1 to 6 packed RBCs. Mean hospital stay was 18.55 ± 4.69 days.

Table 3: Clinical characteristics among studied patients

Variable	N	%
Number of valves replaced		
1	45	81.8%
2	10	18.2%
Locations of valves replaced		
Aortic	15	27.3%
Mitral	30	54.5%
Both	10	18.2%
	Mean ± SD	**Range**
Duration since cardiac surgery (years)	9.25 ± 5.47	1 - 21
Warfarin dose during pregnancy (mg)	6.58 ± 2.28	4 – 12.5
Total daily dose of heparin (IU)	32818 ± 10330	15000 – 60000
Intraoperative blood loss (ml)	460.55 ± 176.7	200 - 1050
Blood loss in 1st 24 hours (ml)	107.31 ± 163.2	0 – 1003
Total blood loss (ml)	812.55 ± 492.2	335 – 2602
Number of packed RBCs transfused	0.4 ± 1.5	1 – 6
Duration since delivery till reaching therapeutic INR	11.65 ± 2.63	9 – 20
Hospital stay (days)	18.55 ± 4.69	13 – 35

RBCs: red blood cells, INR: International normalized ratio

Table 4 shows that 1ry postpartum haemorrhage was found in one patient, intraperitoneal haemorrhage was found in two patients, SC hematoma was found in 3 patients, and SR hematoma was found in 3 patients. While no cases of valve thrombosis or other thromboembolic events were reported. NO maternal death was documented. SC hematoma started with mean of 14.45 cm^2 and reached 8.43 cm^2 on day 14. While SR hematoma started with mean of 33.04 cm^2 and reached 11.81 cm^2 on day 14. Mean of biggest hematoma size recorded was 6.1 cm and ranged from 3 – 10.

Table 4: Outcome and complications among studied patients.

Variable	N	%
1ry postpartum hemorrhage	1	1.8%
Intraperitoneal hemorrhage	2	3.6%
SC hematoma	3	5.5%
SR hematoma	3	5.5%
Reoperation/intervention,		
Re-exploration	1	1.8%
Wound hematoma evacuation	1	1.8%
	Mean ± SD	**Range**
Starting day of hematoma formation or IP hemorrhage	4.57 ± 4.28	2 - 14
SC hematoma size on starting (cm^2)	14.45 ± 17.89	2.34 – 35
SC hematoma size on day 7 (cm^2)	12.09 ± 12.92	4.16 – 27
SC hematoma size on day 14 (cm^2)	8.43 ± 10.18	1.7 – 20.14
SR hematoma size on starting (cm^2)	33.04 ± 34.1	2.86 – 70
SR hematoma size on day 7 (cm^2)	20.18 ± 17.68	2.25 – 37.6
SR hematoma size on day 14 (cm^2)	11.81 ± 11.39	1.44 - 24
Biggest hematoma size (cm)	6.1 ± 3.05	3 – 10

IP: intraperitoneal, SR: sub-rectus, SC: subcutaneous

Discussion

Many of the prosthesis-related complications in the pregnant women can be prevented by careful medical management and follow-up. During pregnancy, mechanical heart valves relate to an increased incidence of thromboembolic events and therapeutic anticoagulants are required to lower the risk of such events [11].

Patients of reproductive age with mechanical prosthetic valves have special challenges due to the lack of an anticoagulant deemed totally safe during all phases of pregnancy. Each anticoagulant has disadvantages, including an increased risk of bleeding or thrombosis, or both [12].

Women with prosthetic mechanical valves that function properly can successfully bear pregnancy. Pregnancy relates to an estimated 29 % increase in

maternal risk, with a maternal death rate of 2.9%. This risk is dependent on the anticoagulant regimen utilized during pregnancy and the anticoagulation quality control[13].

Warfarin offers effective protection against thromboembolism; however, its utilization during pregnancy is associated with an increased abortion rate and the risk of embryopathy induced by warfarin. Due to its potential to pass the placental barrier, warfarin poses a teratogenic risk, especially in early pregnancy. Among the fetal consequences of warfarin are spontaneous abortion, fetal malformation, stillbirth, preterm, retro-placental and cerebral hemorrhage[14].

This issue is especially particular importance in Egypt. A disproportionately high proportion of women of childbearing age have mechanical heart valves, as rheumatic fever and accompanying valvular heart disease continue to be prevalent and severely impact the young. In addition, there is a considerable deal of social pressure to have children despite the danger of illness and death, as many couples, particularly those from lower socioeconomic strata, consider reproduction as the main purpose of marriage [15].

In this study we found that 81.9% of the patients had one valve replaced, and 18.2% of the patients had two valves replaced. 54.5% of the patients had mitral replaced, 27.3% had aortic replaced, and 18.2% had both mitral and aortic replaced. Mean Warfarin dose during pregnancy was 6.58 mg and mean Total daily dose of heparin was 32818 IU. Moreover, mean total blood loss was 812.55 ml and amount of blood transfused was 1 to 6 packed RBCs. Mean hospital stay was 18.55 ± 4.69 days.

This comes in accordance with a study done by Ayad et al.[16]which included (60/100) (60%) patients with (MVR), (22/100) (22%) patients with (AVR), and (18/100) (18%) patients with (DVR).

Hussein et al.[15]found that regarding the type of the metallic prosthetic heart valve in the study group, in this study women with mitral valve replacement (MVR) were (73/119) (61.3%), with aortic valve replacement (AVR) were (24/119) (20.1%), and with double valve replacement (DVR) were (22/119) (18.6%).

This comes also in accordance with a study done by Zeniab et al.[17] which included (64%) with (MVR), (18%) with (AVR), (18%) with (DVR), but in difference to a study done by Cotrufo et al.[18] in which there were 53 pregnancies in 47 women with mitral prosthetic valves only

In this study we illustrated that 1ry postpartum haemorrhage was found in one patient, intraperitoneal haemorrhage was found in two patients, SC hematoma was found in 3 patients, and SR hematoma was found in 3 patients. While no cases of valve thrombosis or other thromboembolic events were reported. NO maternal death was documented. SC hematoma started with mean of 14.45 cm^2 and reached 8.43 cm^2 on day 14. While SR hematoma started with mean of 33.04 cm^2 and reached 11.81 cm^2 on day 14. Mean of biggest hematoma size recorded was 6.1 cm and ranged from 3 – 10.

Van Hagen et al. [19] revealed that 23.1 % of patients with an MHV, 5.1 % of patients with a tissue heart valve & 4.9 % of patients without a prosthetic valve experienced hemorrhagic events.

Hussein et al.[15]found that thrombotic complication was higher with (heparin-warfarin-heparin) (4/71) (5.6%), and heparin (1/20) (5%), p-value (NS). Stuck valve occurred with (1/20) (5%) (Heparin), and (heparin-warfarin-heparin) (2/71) (2.8%), p value (NS), both thrombotic and haemorrhagic complications were absent with (warfarin).

This comes in line with a study done by Zeinab et al.[17], they found that all thromboembolic complications occurred with (heparin) therapy and absent with (warfarin) (9/100) (9%) with significant (p=0.02), and also this comes in accordance with a study done by Cotrufo et al.[18] in which they did not find haemorrhagic complication with warfarin.

In a study done by Niloufar et al.[20], they found that the incidence of thrombosis and haemorrhage was 30% with heparin group, compared with 2.3% in the warfarin group during the 1sttrimester of pregnancy. Also, they found that 90.7% pregnancies in warfarin group I and 50% in heparin warfarin heparin group II had no complications, and our results also supported with a study done by Niloufar et al. [20] in which they found less complications with (warfarin) (5/38) (13.25%), and higher complications with (heparin-warfarin-heparin) (5/11) (45.4%) with significant p=(0.004).

Conclusions: Women with prosthetic heart valves who are of childbearing age should be counseled (preferably before conception) about the potential complications that may emerge during pregnancy. The incidence of 1ry postpartum hemorrhage in individuals receiving Warfarin is roughly 1.8%; according on the existing data, Warfarin is the optimal choice during pregnancy for patients with mechanical heart valves.

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Conflict of Interest: Nil

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