The Choices of Anticoagulants and their Effects on Pregnant Women with Metallic Prosthetic Heart Valves

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Abstract

Background: The management of a pregnant woman who has a metallic prosthetic heart valve requires important considerations especially for maintaining anticoagulation treatment and this represents a real challenge for the medical staff. Patients with mechanical valve prostheses are at high risk for thromboembolic events, valve thrombosis and mortality increases during pregnancy.

Aim of Study: This study attempted to find the maternal outcome in pregnant women with prosthetic heart valve as regard to the choices of regimens of anticoagulation and comparing between warfarin and heparin regimens throughout pregnancy and the better choices of the anticoagulant treatment.

Patients and Methods: This study is case series, interventional study which was done on pregnant women with metallic prosthetic heart valves. These women were presented to Kasr El Aini Cairo University Hospital in the high risk pregnancy unit over duration of three years (from the first of January 2013 to the end of December 2015). Including (112 women (119 pregnancies) with mechanical prosthetic heart valve; mean age was $(29.13 \pm 5.3$ years old). The anticoagulation regimens used from the 1st trimester in women with prosthetic metallic heart valves once they get pregnant were as following; (71/119) of pregnancies were on (heparin-warfarin-heparin) regimen, (20/119) pregnancies were on heparin regimen, and 28/119 pregnancies were on oral anticoagulant (warfarin).

Results: The regimen (heparin warfarin heparin) has less maternal complications (31%) than warfarin (64.3%) and heparin (45%), however both (heparin warfarin heparin) regimen and (heparin) regimen were not protective against thrombotic complications which were (5.6%) (5%) respectively. Postpartum hemorrhage (PPH) was higher in cases used warfarin regimen (28.6%) with significant p-value (0.047), Women with prosthetic heart valves were liable to have high rate of fetal complications (52.1%) either due to anticoagulation treatment during pregnancy or due to cardiovascular impairment which also increase during pregnancy. However the regimen of (heparin-warfarin-heparin) seems to have the highest living birth rate (59/71) (83%) than both heparin alone (10/20) (50%) and warfarin alone (13/28) (46.4%) with significant p-value (0.002).

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Conclusion: A mechanical heart valve is intended to replace a diseased heart valve with its prosthetic equivalent. The number of the pregnant women with metallic prosthetic valve increases and this necessities the need for proper follow-up of them, with concentration on the choices of anticoagulants to prevent valve thrombosis and follow-up of the mother and the fetus. Warfarin is the most protective anticoagulant for the mother, but mostly associated with lower live birth rate.

Key Words: *Pregnancy – Prostheticmetallic – Heart valves – Anticoagulants.*

Introduction

RHEUMATIC fever (RF) and rheumatic heart disease (RHD) is still a major health problem, comprising 56-89% of all cardiovascular diseases in pregnancy & 0.6% of pregnancies of black women in Africa with maternal mortality rate 9.5% [1]. Poor socio-economic standards and difficulty of reaching proper primary health care facilities are the main causes of the high prevalence. Valvular heart disease can be acquired or congenital [2]. A large number of patients with valvular heart disease will be of childbearing age. A mechanical heart valve is intended to replace a diseased heart valve with its metallic prosthetic equivalent [3]. Mechanical prostheses carry specific risks during pregnancy [4]. In Egypt, large number of women of childbearing age have mechanical valves, because of rheumatic fever and concomitant valvular heart disease. Moreover, there is great social pressure to produce children despite the risk of illness and death, because many couples, see childbearing as the sole purpose of marriage [5].

Patients and Methods

This study enrolled all women who were presented to Kasr El Aini Cairo University Hospital in the high risk pregnancy unit over duration of three years (from the first of January 2013 to the end of December 2015). We prospectively fol-

lowed-up 119 pregnancies in 112 women with prosthetic heart valve, presented to the high risk pregnancy unit in their first trimester; they were either as outpatients in its clinic or admitted as inpatients for various obstetric & cardiac indications.

Results

The results of this work will be summarized in the following Tables and Figures.

Table (1): Shows age of the study group.

	Age (groups)	n=119	(100%)
	18y - 25y	32	26.9
	26y - 30y	41	34.5
Age range in years(y) (18-42)	31y - 35y	27	22.7
	36y - 42y	19	16.0
Mean age in years ± SD	29.04±5.21		

Table (2): Characteristics of the study group.

	n=119	(100%)
Smoking	0	0
Pre pregnancy counseling:		
Yes	63	52.9
No	56	47.1
Compliance to warfarin treatment before pregnancy	118	99.1
Hypertension	1	0.84
Atrial fibrillation	16	13.4
Anti-phospholipid syndrome	1	0.84
History of abortion before valve replacement	14	11.7
History of abortion after valve replacement	67	56.3

Table (3): Shows cardiac surgical history of the study group.

Type of replaced heart valve	n=119	(100%)
Mitral valve replacement (MVR)	73	61.3
Aortic valve replacement (AVR)	24	20.1
Double valve replacement (DVR)	22	18.6
Frequency of recurrent cardiac surgery:		
Once	5	4.2
Twice	1	0.84
Three	2	1.68
Cause of recurrent cardiac surgery:		
Stuck valve	15	12.6
Non-fitting prosthesis	13	10.9
Surgical valve repair	1	0.84

There were 14 women admitted to ICU (intensive care unit) and indications were as following; 10 women with heart failure after delivery, 3 women with stuck valves (two during pregnancy with stuck valve at (11, 12 weeks of pregnancy respectively and one woman with stuck valve after delivery), and one woman admitted to ICU due to major postpartum hemorrhage.
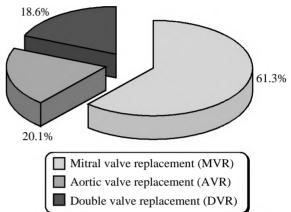

Fig. (1): Shows the type of replaced valve in the study group.

Table (4): Shows the anticoagulation regimens used in pregnancy in the study group.

Anticoagulation regimens	n=119	(100%)
Heparin → Warfarin → Heparin	71	59.6
Warfarin throughout pregnancy	28	23.5
Heparin throughout pregnancy	20	16.9

The study group was divided according to the regimen of anticoagulation used into main three groups: First group used (heparin-warfarin-heparin) regimen. The first group was subdivided into two subgroups: Those used (Cal heparin-warfarin-Cal heparin) (32) and those used (Na heparin-warfarin-Na heparin) (39) cases. Second group used (warfarin) regimen. Third group used (heparin) regimen. The third group was subdivided into two sub groups: Those used (Cal heparin) (10) and those used (Na heparin) (10) cases. There were two cases on LMWH (clexan) but as a result to the difficult monitoring they shifted to intravenous sodium heparin then subcutaneous heparin according to their APTT laboratory results.

NB the cases were taking sodium heparin by subcutaneous (SC) route except when admitted to the high risk pregnancy unit they were taking it intravenously for proper control of anticoagulation and shifted to (SC) route on discharge.
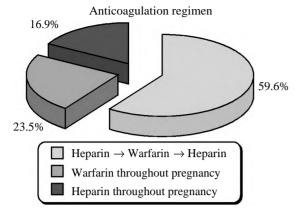
Anticoagulation regimen

Fig. (2): Shows the anticoagulation regimens used in pregnancy in the study group.

Table (5): Shows clinical characteristics of the study group.

	Mean ± SD
Mean systolic blood pressure	115.08±7.81
Mean diastolic blood pressure	71.76±7.82
Uterine Blood Flow (done at 18-22) week of pregnancy:	
Mean uterine Pulsatory index (PI)	0.80±0.15
Mean uterine Resistance index (RI)	0.62±0.15

Mean uterine pulsatory index (PI) was higher (0.80±0.15) than normal levels (0.63±0.19), mean uterine resistance (RI) index was high (0.62 ± 15) than normal (0.44±0.09).

Table (6): Shows maternal outcomes in the study group.

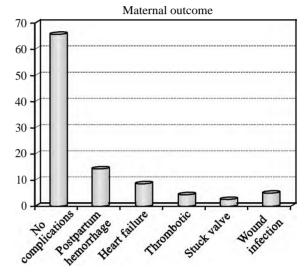| Maternal outcomes	n=119	(100%)
No complications	78	65.5
Maternal complications	41	34.5
Postpartum hemorrhage (PPH)	17	14.3
Heart failure	10	8.5
Thrombotic complication	5	4.2
Stuck valve	3	2.5
Wound infection	6	5

Fig. (3): Shows maternal outcomes in the study group.

Relations:

Table (7): Shows relation between the mode of delivery and regimens of anticoagulation in the study group.

	Regimen of anticoagulation			Total n=95 (100%)	*p*-value
	Heparin-warfarin-Heparin n=(67)	Warfarin n=(16)	Heparin n=(12)		
Mode of Delivery: *Vaginal:*					
N	52	7	4	63	0.001*
%	77.6	43.5	33.3	66.3	
CS:					
N	15	9	8	32	
%	22.4	56.5	66.7	34.7	

Cases delivered by normal vaginal delivery were (63) and cases delivered by CS delivery were (32) and D&C cases were 24. There is statistical significance between normal vaginal delivery and regimens of anticoagulation, normal vaginal delivery was higher with (heparin-warfarin-heparin) (52/67) (77.6%), and least with warfarin (7/16) (43.5%) and (heparin) (4/12) (33.3%) with significant *p*-value (0.001). There is statistical significance between the regimens of anticoagulation and CS delivery, CS delivery was higher with (heparin) (8/12) (66.7%) and (warfarin) (9/16) (56.5%), lesser with (heparin-warfarin-heparin) (15/67) (22.4%) with significant *p*-value (0.001).
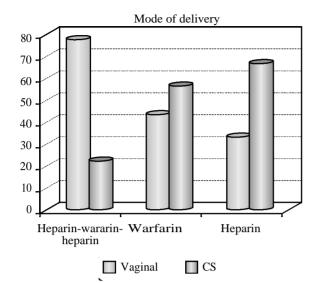
Mode of delivery

Fig. (4): Shows relation between the mode of delivery and regimens of anticoagulation in the study group.

Table (8): Shows relation between the regimen of anticoagulation and D&C operations.

	Regimen of anticoagulation				
	Heparin-warfarin-Heparin n=4	**Warfarin** n=12	Heparin n=24	Total n=24	*p*-value
D&C: N %	16.6%	50%	33.4%	20.2%	0.001*

There is statistical significance between the regimen of anticoagulation and D&C operation. D&C operation was higher with warfarin regimen (12/24) (50%), lesser with heparin (8/24) (33.3%) and least with heparin-warfarin-heparin (4/24) (16.6%) with significant *p*-value 0.001.

Table (9): Shows relation between the mode of delivery and type of the replaced heart valve in the study group.

	Replaced heart valve			Total n=95 (100%)	*p*-value
	AVR (20)	MVR (56)	DVR (19)		
Mode of Delivery : *Vaginal:* N %	17 85	43 76.7	3 15.7	63 66.3	0.001*
CS: N %	3 15	13 23.3	16 84.3	32 33.7	

There is statistical significance between the type of replaced heart valve and normal vaginal delivery which was higher with AVR (17/20) (85%)

and with MVR (43/56) (76.7%) and least with DVR (3/19) (15.7%) with significant *p*-value (0.001). There is statistical significance between CS deliveries and type of valve replacement, CS deliveries were higher in women with double DVR (16/19) (84.3%) lower with MVR (13/ 56) (23.3%) and AVR (3/20) (15%) with significant *p*-value (0.001).
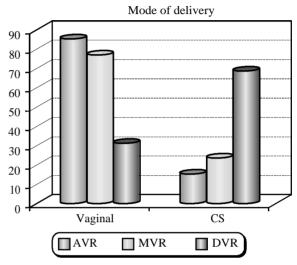
Mode of delivery

Fig. (5): Shows relation between the mode of delivery and type of the replaced heart valve in the study group.

Table (10): Shows relation between maternal out comes and regimens of anticoagulation in the study group.

	Regimen of anticoagulation			Total n=119 (100%)	*p*-value
	Heparin-warfarin-Heparin (71)	Warfarin (28)	Heparin (20)		
Maternal outcomes: *No complications:* N %	49 69%	18 64.3%	11 55.0%	78 65.5%	0.501
PPH: N %	7 9.9%	8 28.6%	2 10.0%	17 14.3%	0.047*
Heart failure: N %	7 9.9%	0 0%	3 15.0%	10 8.5%	0.143
Thrombotic complication : N %	4 5.6%	0 .0%	1 5.0%	5 4.2%	0.445
Wound infection: N %	2 2.8%	2 7.1%	2 10.0%	6 5.0%	0.364
Stuck valve: N %	2 2.8%	0 .0%	1 5%	3 2.5%	0.716

There was statistical significance between the regimen of anticoagulation and (PPH) which was higher with (warfarin) (8/28) (28.6%), lesser with (heparin) (2/20) (10%), and least with (heparin-warfarin-heparin) (7/71) (9.9%), with significant *p*-value (0.047). There was no statistical significance between and the regimen of anticoagulation and the rest of maternal outcomes, best outcome was with (heparin-warfarin-heparin) (49/71) (69%), followed by (warfarin) (18/28) (64.3%), lastly (heparin) (11/20) (5 5%), *p*-value (NS). Heart failure complication was higher with (heparin) (3/20) (15%), lower with (heparin-warfarin-heparin) (7/71) (9.9%), and absent with (warfarin), *p*-value (NS). Thrombotic complication was higher with (heparin-warfarin-heparin) (4/71) (5.6%), and lower with heparin (1/20) (5%), *p*-value (NS). Stuck valve occurred with (1/20) (5%) (Heparin), and with (heparin-warfarin-heparin) (2/71) (2.8%), both thrombotic and stuck valve complications were absent with (warfarin), *p*-value (NS).
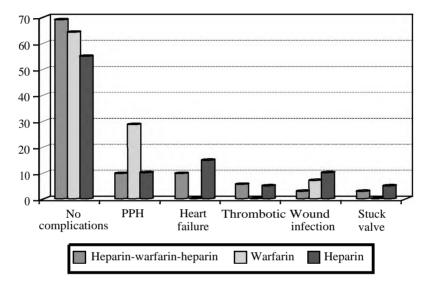

Fig. (6): Shows relation between maternal outcomes and regimens of anticoagulation in the study group.

Table (11): Shows relation between maternal outcomes and the type of replaced heart valve in the study group.

	Replaced heart valve			Total n=119 (100%)	*p*-value
	AVR (24)	MVR (73)	DVR (22)		
Maternal outcomes:					
No complications:					
N	18	48	12	78	0.345
%	75.0%	65.8%	54.5%	65.5%	
PPH:					
N	1	12	4	17	0.279
%	4.2%	16.4%	18.2%	14.3%	
Heart failure:					
N	4	3	3	10	0.024*
%	16.6%	4.1%	13.6%	8.5%	
Thrombotic complication:					
N	0	4	1	5	0.434
%	.0%	5.5%	4.5%	4.2%	
Wound infection:					
N	0	4	2	6	0.358
%	.0%	5.5%	9.1%	5.0%	
Stuck valve:					
N	1	2	0	3	0.771
%	4.2%	2.7%	.0%	2.5%	

There was statistical significance between the type of replaced heart valve and heart failure complication, which was higher with AVR (4/24) (16.6%) and DVR (3/22) (13.6%), and least with MVR (3/73) (4.1%) with significant p-value (0.024). Postpartum hemorrhage was higher with DVR (4/22) (18.2%), and in MVR (12/73) (16.4%), least with AVR (1/24) (4.2%). Thrombotic compli-

cation was higher in MVR (4/73) (5.5%), lower with DVR (1/22) (4.5%), and absent with AVR. Wound infection was higher with DVR (2/22) (9.1%), lower with MVR (4/73) (5.5%), absent with AVR. Stuck valve complication was higher with AVR (1/24) (4.2%), lower with MVR (2/73) (2.7%), and absent with DVR. p-value (NS).
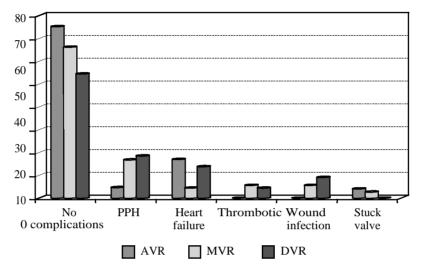

Fig. (7): Shows relation between maternal outcomes and the type of replaced heart valve in the study group.

Table (12): Shows relation between maternal complications and the time lapse from valve replacement till pregnancy.

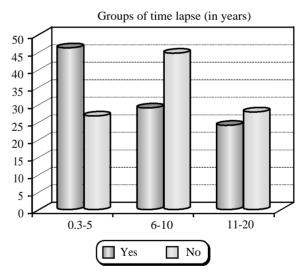| Time lapse Range (0.3-20) years	Maternal complications		Total n=119 (100%)	p-value
	Yes (41)	No (78)		
Groups of Time lapse (in years):				
0.3-5:				
N	19	21	40	0.033*
%	46.3%	26.9%	33.6%	
6-10:				
N	12	35	47	0.097
%	29.3%	44.9%	39.5%	
11-20:				
N	10	22	32	0.656
%	24.4%	28.2%	26.9%	

Fig. (8): Shows relation between maternal complications and the time lapse from valve replacement till pregnancy.

There was statistical significance between maternal complications and time lapse from prosthetic metallic valve replacement surgery to occurrence of pregnancy in the study group. Higher maternal complications occurred in time lapse (0.3-5) years in (19/41) (46.3%) with significant p-value (0.033). least maternal complications in time lapse (11-20) years in (10/41) (24.4%) women p-value (NS).

Discussion

Many of the prosthesis-related complications in the pregnant women can be prevented by careful medical management and follow-up. Mechanical heart valves are associated with an increased incidence of thromboembolic events during pregnancy. Therapeutic anticoagulation throughout pregnancy

is essential to reduce the risk of thromboembolic complications [6].

Patients of childbearing age with mechanical prosthetic valves pose unique challenges since there is no optimal anticoagulation agent considered completely safe at all stages of pregnancy. Each anticoagulant option has its drawbacks, whether increased risk of bleeding, increased risk of thromboembolism, or both [7].

In women with well-functioning mechanical valves prosthesis they can tolerate pregnancy well. Pregnancy is associated with increased maternal risk estimated to be as high as 29% with a 2.9% maternal mortality rate. This risk depends on the anticoagulation regimen used during pregnancy and the quality of anticoagulation control [8].

Warfarin provides effective protection against thrombo-embolism, but its use in pregnancy is associated with an augmented rate of abortion and the risk of warfarin-induced embryopathy. Warfarin has a teratogenic risk because of its ability to cross the placental barrier, particularly during early gestational age. Fetal complications of warfarin include: Spontaneous abortion, prematurity, fetal deformity, stillbirth, retro-placental hemorrhage and intracranial hemorrhage [9].

Unfractionated heparin (UFH) provides an alternative therapy that avoids fetal side effects; however, the use of UFH is associated with increased maternal thrombo-embolic and bleeding complication [10].

Low molecular weight heparin (LMWH) may be more advantageous than UFH and appears a good alternative; however scant information has been published on the use of LMWH in pregnant women with prosthetic heart valves [11].

In Egypt, this problem is of particular importance. An unusually large number of women of childbearing age have mechanical valves, because rheumatic fever and concomitant valvular heart disease are still common and affect the young most severely. Moreover, there is great social pressure to produce children despite the risk of illness and death, because many couples, especially in the lower socioeconomic classes, see childbearing as the sole purpose of marriage [5].

The current study is case series and interventional study. We prospectively followed-up 119 pregnancies in 112 women with mechanical prosthetic cardiac valves presented to the high risk pregnancy unit at Kasr Al Aini Cairo University Hospital (from the first of January 2013 to the end of December 2015). Pregnant women presented in the first trimester of their pregnancy, they were either as outpatients in its clinic or admitted as inpatients for various obstetric & cardiac indications. This study is an attempt to identify the best anticoagulant regimen for pregnant women with metallic heart valve prostheses with less maternal and fetal complications.

Revising the demographic data of the studied population, in the current study, the total number of cases was 112 women with 119 pregnancies with mean ages (29.04±5.21) years, age range (18-42). In accordance to a study done by [5], the mean age at pregnancy was (25.32±4.4) and age range (19-45) years.

The mode of delivery in the study group was mainly vaginal (52.9%) and caesarion deliveries were (26.6%), this comes indifference with a study done by [12], in which they foundcaesarean section was the predominant method of delivery in patients as opposed to controls (55%).

Revising the clinical characteristics of the study group; uterine doppler (done at 18-22 week of pregnancy), it was found in this study that: Mean uterine pulsatory index (PI) was higher (0.80±0.15) than normal levels (0.63±0.19), mean uterine resistance (RI) index was high (0.62±15) than normal (0.44±0.09).

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 in accordance to a study done by [13], which included (60/100) (60%) patients with (MVR), (22/100) (22%) patients with (AVR), and (18/100) (18%) patients with (DVR). This comes also in accordance to a study done by [5], which included (64%) with (MVR), (18%) with (AVR), (18%) with (DVR), but in difference to a study done by [14] in which there were 53 pregnancies in 47 women with mitral prosthetic valves only.

Regarding the anticoagulation regimen used from the first trimester and throughout pregnancy till abortion or delivery. The study group was divided into three groups: Group (I) women used (heparin-warfarin-heparin) regimen (71/119) (59.6%), group (II) women used (warfarin) regimen (28/119) (23.5%) and group (III) women used (heparin) regimen (20/119) (16.9%), this comes in accordance to a study done by [4], but in difference

to a study done by [14], this study was done only on two groups divided according to the regimen of anticoagulation used from the first trimester into group (I) women used (heparin-warfarin-heparin) regimen and group (II) women used (warfarin) regimen and not including heparin regimen.

Relations:

As regard the relation between the regimen of anticoagulation and maternal deaths, in this study no maternal deaths occurred, this comes in accordance to a study done by (Cotrufo) [15] and (Chan) [4], but comes in difference to a study done by (Niloufar) [14] in which they found (1/53) of maternal death (1.9%) and indifference with a study done by (Zenab) [5] maternal deaths were (4/100) (4%).

Regarding the relation between mode of delivery and regimen of anticoagulation used during pregnancy in the study group. In this study, normal vaginal delivery was statistically higher especially with (heparin-warfarin-heparin) (52/67) (77.6%) and least with warfarin (7/16) (43.5%) and (heparin) (4/12) (33.3%). CS delivery was higher with (heparin) (8/12) (66.7%) and (warfarin) (9/16) (56.5%), lesser with (heparin-warfarin-heparin) (15/67) (22.4%) with significant p-value (0.001). This comes in accordance to a study done by (Niloufar) [14] ceasarean section was higher (66.7%) than vaginal deliveries (33.3%) in group I (warfarin), and in difference with the same study as ceaserion delivery was higher (71.4%) than vaginal delivery (28.6%) in group II (heparin warfarin heparin).

As regard the relation between the mode of delivery and type of the replaced prosthetic metallic heart valve in the study group. In this study, normal vaginal delivery which was higher with AVR (17/20) (85%) and with MVR (43/56) (76.7%) and least with DVR (3/19) (15.7%). CS deliveries were higher in women with double DVR (16/19) (84.3%) lower with MVR (13/ 56) (23.3%) and AVR (3/20) (15%) with significant p-value (0.001).

Regarding the relation between maternal outcomes and the regimen of anticoagulation used during pregnancy in the study group. In this study no complications in (78/119) (65.5%), best outcomes were with (heparin-warfarin-heparin) (49/71) (69%), followed by (warfarin) (18/28) (64.3%), and lastly with (heparin) (11/20) (55%), p-value (NS), this comes in difference with a study done by (Niloufar) [14] (90.7%) pregnancies in group I (warfarin) and (50%) in group II (heparin warfarin heparin) had no complications (p-value=0.001),

and also in difference with a study done by (Amir) [16], 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).

In this study, Postpartum hemorrhage was higher with (warfarin) (8/28) (28.6%), lesser with (heparin) (2/20) (10%), and (heparin-warfarin-heparin) (7/71) (9.9%), with significant p-value (0.047), PPH was (14.3%) in the study group, this comes in accordance with a study done by (Chan) [4] Major bleeding events occurred in 2.5% of all pregnancies, most at the time of delivery, but comes in difference with a studies done by (Vitale) [17] and (Cotrufo) [15] they did not find postpartum hemorrhage.

In this study heart failure was higher with (heparin) (3/20) (15%), lower with (heparin- warfarin-heparin) (7/71) (9.9%), and absent with (warfarin), p-value (NS), this comes in accordance to a study done by (Ayad) [13], in which they found that patients on heparin developed more heart failure.

In this study, 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 stuck valve complications were absent with (warfarin), this comes in accordance with a study done by (Zeinab) [5], 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) [15], in which they did not find thrombotic complication with warfarin, but in difference with a study done by (Niloufar) [14], in which they found that the incidence of valvular thrombosis was 30% with heparin group, compared with 2.3% in the warfarin group during the first trimester of pregnancy.

As regard the relation between maternal complications and type of replaced heart valve in the study group. In this study, heart failure complication was higher with AVR (4/24) (16.6%), and with DVR (3/22) (13.6%), and least with MVR (3/73) (4.1 %) with significant p-value (0.024).

Postpartum hemorrhage was higher with DVR (4/22) (18.2%), and with MVR (12/73) (16.4%), least with AVR (1/24) (4.2%), this comes in difference with a study done by (Ayad) [13], in which they found that, postpartum hemorrhage was more common with AVR than MVR, (p=NS).

In this study, thrombotic complication was higher with MVR (4/73) (5.5%), lower with DVR (1/22) (4.5%), and absent with AVR, p-value (NS), this comes in accordance to a study done by (Ayad) [13] thrombosis occurred more frequently in patients with (MVR).

In this study, Wound infection was higher with DVR (2/22) (9.1%), lower with MVR (4/73) (5.5%), absent with AVR. Stuck valve complication was higher with AVR (1/24) (4.2%), lower with MVR (2/73) (2.7%), and absent with DVR, p-value (NS).

As regard the relation between maternal complications and time lapse from prosthetic metallic valve replacement surgery to occurrence of current pregnancy in the study group. In this study, higher maternal complications (19/41) (46.3%) occurred with the shortest time lapse (0.3-5) years with significant p-value (0.033). Least maternal complications occurred with the longest time lapse (11-20) years in (10/41) (24.4%) women p-value (NS), this comes in accordance to a study done by (Zeinab) [5].

As regard the relation between maternal complications and the type of replaced metallic prosthetic heart valve in the study group. In this study, higher maternal complications were present with DVR (10/22) (45.5%), lesser with MVR (25/73) (34.2%), and least with AVR (24/24) (34.2%). p-value (NS), this comes in accordance with a study done by (Eulogio) [18], in which they found that patients with isolated aortic valve replacement had fewer maternal complications (2/13) than patients with isolated mitral valve replacement (15/42) without statistical significance.

References

1- STANGL V., SCHAD J., GOSSING G., BORGES A., BAUMANN G. and STANGL K.: Maternal heart disease and pregnancy outcome: A single-centre experience. J. Heart Failure, 10: 855-860. 12, 2008.

2- DRENTHEN W., BOERSMA E., BALCI A., MOONS P., ROOS-HESSELINK J.W., MULDER B.J., VLIEGEN H.W., VAN DIJK A.P., VOORS A.A., YAP S.C., VAN VELDHUISEN D.J. and PIEPER P.G.: Predictors of pregnancy complications in women with congenital heart disease. Eur. Heart J., 31: 2124-2132, 2010.

3- ROSS M.G. and BEALL M.H.: Adult sequelae of intrauterine growth restriction. Semin Perinatol., 32: 213-8, 2008.

4- CHAN W.S., ANAND S. and GINSBERG J.S.: Anticoagulation of pregnant women with mechanical heart valves: A systematic review of the literature. Arch. Intern. Med., 160: 191-196, 2013.

5- ZEINAB ATTIA ASHOUR, HESHAM ABDEL FATTAH SHAWKY and MOHAMED HASSAN HUSSEIN: Outcome of Pregnancy in Women with Mechanical Valves; Tex Heart Inst. J., 27 (3): 240-245, 2000.

6- BATES S.M., GREER I.A., MIDDELDORP S., et al.: VTE, thrombophilia, antithrombotic therapy, and pregnancy: Antithrombotic Therapy and Prevention of Thrombosis. American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. Chest, 141: e691S, 2012.

7- CASTELLANO, RAJEEV L. NARAYAN, PRASHANT VAISHNAVA and VALENTIN: Fuster Nature Reviews Cardiology, 9: 415-424 (July 2012) doi: 10. 103 8/nrcardio. 2012.69

8- ABILDGAARD U., SANDSET P.M., HAMMERSTROM J., GJESTVANG F.T. and TVEIT A.: Management of pregnant women with mechanical heart valve prosthesis: Thromboprophylaxis with low molecular weight heparin. Thromb. Res., 124: 262-267, 2009.

9- Can Fam Physician. Prosthetic heart valves and management during pregnancy, Feb. 55 (2): 155-157, 2009.

10- NASSAR A.H., HOBEIKA E.M., ABD ESSAMAD H.M., TAHER A., KHALIL A.M. and USTA I.M.: Pregnancy outcome in women with prosthetic heart valves. Am. J. Obstet Gynecol., Am. Usta I.M., 191 (3): 1009-1013, 2004.

11- GREER I.A. and NELSON-PIERCY C.: Low-molecular-weight heparins for thromboprophylaxis and treatment of venous thromboembolism in pregnancy: A systemic review of safety and efficacy. European Society of Gynecology (ESG), Association for European Paediatric Cardiology (AEPC), German Society for Gender Medicine (DGesGM), et al. ESC Guidelines on the management of cardiovascular diseases during pregnancy: The Task Force on the Management of Cardiovascular Diseases during Pregnancy of the European Society of Cardiology (ESC). Eur. Heart J., 32: 3147.005; 106 (2): 401-407, 2011.

12- SILLESEN M., HJORTDAL V., VEJLSTRUP N. and SØRENSEN K.: Pregnancy with prosthetic heart valves - 30 years' nationwide experience in Denmark. Eur. J. Cardiothorac. Surg., 40: 448, 2011.

13- AYAD et al.: Maternal and Fetal Outcomes in Pregnant Women with a Prosthetic Mechanical Heart Valve. Clinical Medicine Insights: Cardiology, 10: 11-17, 2016. doi: 10.4137/CMC.S36740

14- NILOUFAR SAMIEI, FAHIMEH KASHFI, AMIRJAMSHID KHAMOUSHI, SAEID HOSSEINI, ALIREZA ALIZADEH GHAVIDEL, ROBABEH TAHERIPANAH and YALDA MIRMESDAGH: Pregnancy Outcome after Mechanical Mitral Valve Replacement: A Prospective Study Tehran Heart Cent., Aug. 7 (3): 117-120, 2012.

15- COTRUFO M., DE FEO M., DE SANTO L.S., ROMANO G., DELLA CORTE A., RENZULLI A. and GALLO C.: Risk of warfarin during pregnancy with mechanical valve prostheses. Obstet. Gynecol., 99: 35-40, 2002.

16- AMIRJAMSHID KHAMOUSHI, SAEID HOSSEINI, ALIREZA ALIZADEH GHAVIDEL, ROBABEH TAHERIPANAH and YALDA MIRMESDAGH: Pregnancy Outcome after Mechanical Mitral Valve Replacement: A Prospective Study Tehran Heart Cent., Aug. 7 (3): 117-120, 2012.

17- VITALE N1, DE FEO M., DE SANTO L.S., POLLICE
A., TEDESCO N. and COTRUFO: Dose-dependent fetal
complications of warfarin in pregnant women with me-
chanical heart valves, May 33 (6): 1637-41, 1999.

18- EULOGIO E. MARTINEZ, PEDRO A.M. ALMEIDA [a,b],
DIRCEU V. SANTOS [a,b], ANTONIO C.C. CARVALHO,
ANTONIO F. MORON[a], CELIA H. MIYASAKI[a,b],
SERGIO D. MORAES[a,b] and JOHN A. AMBROSE[a,b]:
Regnancy in patients with prosthetic heart valves: The
effects of anticoagulation on mother, fetus, and neonate
Daniel Borna, b, Volume 124, Issue 2, August, Pages 413-
417, 1992.

اختيارات أدوية موانع التجلط وآثارها على الأمهات الحوامل واللائى لديهن صمام معدنى صناعى بالقلب

تعتبر الحمى الروماتيزمية من أسباب الأصابة بتلف فى صمامات القلب فى مصر والعالم النامى، كما أن التلف فى الصمام القلبى قد يكون موروثاً، وفى الحالتين فإن استبدال الصمام التالف بصمام صناعى يكون ضرورياً ليعمل القلب بشكل صحيح، ونتيجة التقدم المستمر فى جراحات القلب المفتوح فقد أصبحت عملية استبدال الصمام التالف تجرى لاناث صغار قبل أو مع سن الإنجاب. لهذا السبب فقد نجد أن نسبة السيدات الحوامل اللائى لديهن صمام صناعى معدنى فى ازدياد وتبع ذلك ضرورة المتابعة الطبية للأمهات الحوامل اللائى لديهن صمام معدنى صناعى بالقلب مع التركيز على مضادات التجلط اللازم استخدامها لمنع التجلط ورصد نتيجة وآثار ذلك على الأم والجنين.

المرضى : أجريت الدراسة على السيدات الحوامل اللائى لديهن صمام صناعى معدنى أو أكثر بالقلب، واللائى يأتين إلى وحدة الحمل الحرج بمستشفى القصر العينى جامعة القاهرة للمتابعة يوم الاثنين اسبوعياً فى العيادة الخاصة بالوحدة، أو اللائى يتم حجزهن بالقسم الداخلى للوحدة لأسباب تتعلق بالقلب أو الحمل. وقد أجريت الدراسة على عدد ١١٩ حالة حمل لعدد ١١٢ سيدة بداية من شهر يناير ٢٠١٣ إلى نهاية شهر ديسمبر ٢٠١٥.

وأساليب البحث : بالنسبة لجميع المرضى تم عمل الآتى :

الحصول على الاستشارة الطبية الازمة لاختيار طريقة العلاج بمانع التجلط على الصمام الصناعى، وقد تم مناقشة ذلك مع الحامل وأحياناً مع الزوج أن وجد معها وذلك فى المرحلة الأولى للحمل.

وقد تم تحديد ثلاثة أنظمة للعلاج لاستخدامها وهى كالتالى :

١– عقار الوارفارين الماريفان أثناء المرحلة الأولى للحمل إلى نهاية المرحلة الأخيرة للحمل مع إيقافه فى الأسبوعين الأخيرين للحمل أو مع حدوث الأم المخاض والولادة.

٢– عقار الهيبارين من بداية المرحلة الأولى للحمل وحتى نهاية الحمل.

٣– عقار الهيبارين من بداية المرحلة الأولى للحمل والأسبوعين الأخيرين للحمل ما قبل الولادة، واستخدام عقار الوارفارين الماريفان فى الفترة التى بينهما.

وبالنسبة للهيبارين فقد نوقش أنه غير آمن على الأم كمانع للتجلط سواء على الصمام المعدنى المستبدل أو فى أى مكان فى الجسم ولكنه آمن على الجنين حيث أنه لا يسبب أى تشوه للجنين وأيضاً فأن استخدام الهيبارين فى بعض الأحيان قد يؤدى إلى حدوث هشاشة العظام ونقص فى عدد الصفائح الدموية وافراز الغدة الفوق كلوية للأم الحامل أو النزف.

فيما يخص التاريخ المرضى : السؤال عن وجود أى أمراض مزمنة كارتفاع الضغط أو مرض السكرى وإجراء أى عمليات جراحية سابقة.

فيما يخص مجال النساء والتوليد : تم السؤال عن تاريخ أول يوم فى آخر دورة شهرية سبقت الحمل وعدد مرات الحمل قبل أو بعد الصمام وعدد مرات الولادة قبل أو بعد الصمام وطريقة الولادة سواء كانت طبيعية أو قيصرية ومكان الولادة، والسؤال عن حدوث ولادة مبكرة أو حدوث مضاعفات فى الاحمال السابقة مثل الاجهاض وعدد مراته أو وفاة الجنين سواء فى رحم الأم أو بعد الولادة أو حدوث تشوهات للاجنة والسؤال عن وجود صلة قرابة بين الأب والأم.

فيما يخص القلب : تاريخ عملية الاستبدال بالصمام الصناعى المعدنى ومكان الصمام الذى تم استبدا له أما ميترالى أو أورطى أو الاثنين معاً، وعدد مرات عمليات القلب المفتوح التى تم أجراؤها والسؤال عن حدوث مضاعفات أثناء أو بعد العملية أو مضاعفات خاصة بالصمام مثل:

حدوث جلطة على الصمام أوفى أى مكان آخر من الجسم وتاريخ حدوثها وآثار ذلك والعلاج الذى تم أخذه أو العمليات التى أجريت. حدوث نزيف نتيجة العلاج بمضادات التجلط والسؤال عن مكان حدوثه فى الجسم وما أن نقل أى من مشتقات الدم و عدد الوحدات المنقولة أن وجد.

وتم متابعة وظائف القلب وذلك من خلال المتابعة مع أطباء قسم القلب والأوعية الدموية بالقصر العينى جامعة القاهرة وعمل فحص إكلينيكى على القلب للاطمئنان على صمامات القلب وأيضاً فحص الصدر والبطن والساقين لتحديد أى علامة لفشل القلب مع الحمل والاطمئنان على ضغط الدم والنبض والحرارة.

وقد تم عمل الفحوصات الآتية :

وبالنسبة للفحوصات المعملية : تم عمل صورة الدم الكاملة، عامل ريسوس، سكر عشوائي، وظائف الكبد والكلى، والتحاليل الخاصة بالسيولة والتجلط مثل زمن ونشاط البروثرومبين الجزئى (APTT) فى حالة استخدام الهيبارين كمانع للتجلط وأيضاً عمل (النسبة الطبيعية المشتركة) (INR) فى حالة استخدام عقار الوارفارين كمانع للتجلط مع المقارنة بالنسب الطبيعية المطلوبة فى حالة الصمام الصناعى.

وبالنسبة للأشعات التشخصية : تم عمل أشعة تليفزيونية على القلب من بداية الحمل، وحسب الاحتياج بعد فحص القلب وفى الشهر التاسع للحمل للحالات التى اكتمل حملها للشهر التاسع وتحديد وجود أى مشكلة فى القلب، وأيضاً تم عمل أشعة تليفزيونية على الرحم لمعرفة عمر الجنين، وجود توأم أو وجود أى مشكلة بالجنين مثل عدم وجود نبض بالجنين، تأخر فى نمو الجنين أو وجود أى تشوهات جنينية. وأيضاً تم عمل أشعة ثلاثية الابعاد بصفة روتينية بداية من الاسبوع العشرين إلى الاسبوع الرابع والعشرين لكل الحالات التى وصل عمر الجنين معها لهذه المرحلة وخصوصاً الحالات التى أخذت عقار الوارفارين الماريفان كمانع للتجلط على الصمام الصناعى مع الحمل وذلك لتحديد أى تشوهات وخصوصاً التى قد تحدث بسبب تعاطى عقار الوارفارين. وكانت عدد مرات المتابعة.

والغرض الأساسى من البحث هو :

معرفة الطريقة الأفضل للعلاج المستخدم فى منع التجلط على الصمام الصناعى المعدنى فى السيدات الحوامل ورصد أى مضاعفات على الام مثل حدوث جلطة على الصمام أو خارج الصمام أثناء الحمل أو الولادة، أيضاً حدوث نزيف مع الحمل أو مع الولادة أو بعد الولادة أو حدوث فشل فى وظائف القلب أو التنفس أو حجز الأم فى العناية المركزة.