

## The Choices of Anticoagulants in Pregnant Women with Metallic Prosthetic Heart Valves and the Fetal Outcome

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### Abstract

**Background:** Patients with mechanical valve prostheses are at high risk for thromboembolic events and mortality increases during pregnancy. The most effective anticoagulation for the mother is achieved with oral anticoagulants which may be associated with embryopathy in the baby. Heparin does not cross the placental barrier and does not cause embryopathy. All forms of unfractionated heparin are associated with a higher rate of maternal complications and death. This study attempted to find the fetal outcome in pregnant women with prosthetic heart valve and comparing between warfarin, heparin or heparin warfarin heparin regimens throughout pregnancy and the best choice between them.

**Aim of Study:** To determine fetal outcomes, true incidence and the clinical impact of warfarin embryopathy and to make sensible recommendations for other future pregnancies as regard the better choice of the anticoagulant regimen.

**Patients and Methods:** This study is case series, interventional prospective 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 ±5.3 years old), evaluating the pregnancy out come as regard; spontaneous abortion, therapeutic abortion due to congenital anomalies, intrauterine fetal death IUFD, neonatal deaths, preterm delivery babies, and low birth weight babies.

**Results:** The anticoagulation regimens used from the 1<sup>st</sup> 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). Pregnancy outcomes of 119 pregnancies were as following, (57/119) resulted in full term babies, which were higher with (heparin-warfarin-heparin) (47/71) (66.2%) *p*-value (0.001). The total live births were higher with (heparin-warfarin-heparin) (59/71) (83%), lower with heparin (10/20) (50%) and least with warfarin (13/28) (46.4%) *p*-value (0.002). Heparin and warfarin regi-

mens were associated with high missed abortion in the first trimester as diagnosed by ultrasound (40%) (35.7%), however due to congenital anomalies which was associated with warfarin dose more than 5mg and therapeutic abortion which was done after that, the rate of abortion with warfarin was (42.9%) with significant *p*-value (0.001). Preterm labor higher with warfarin regimen (25%) with significant *p*-value (0.009). Neonatal deaths were higher with warfarin regimen (10.7%) especially when warfarin dose was more than 5mg with significant *p*-value (0.045).

**Conclusion:** Women with prosthetic heart valves liable to have high rate of fetal complications 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 than both heparin alone and warfarin alone. Both heparin and warfarin regimens were associated with high missed abortion in the first trimester as diagnosed by ultrasound, also neonatal deaths were higher with warfarin regimen especially when warfarin dose was more than 5mg.

**Key Words:** Anticoagulants – Pregnancy – Fetal outcome – Prosthetic – Metallic heart valves.

### Introduction

**WOMEN** with mechanical prosthetic heart valves require lifelong anticoagulation usually with warfarin to prevent valve thrombosis. During pregnancy their thrombotic risk increase estimated to be as high as 29% with a 2.9% maternal mortality rate [1]. 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. First trimester complications of warfarin include: Spontaneous abortion, prematurity, fetal deformity, stillbirth, retro-placental hemorrhage and intracranial hemorrhage [2]. Unfractionated heparin (UFH) provides an alternative therapy that avoids fetal side effects; however, the use of UFH is associated with increased maternal

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thrombo-embolic and bleeding complications [3]. 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 [4].

### Patients and Methods

This study is case series, interventional prospective 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). Patients were divided into three groups, group I (n=71) received heparin in the first trimester of pregnancy, and took warfarin after the first trimester until 36 week then heparin, group II (n=28) took warfarin throughout the pregnancy and group III (n=20) took heparin throughout the pregnancy.

### Results

The result of this work will be summarized in the following tables and figures.

Table (1): 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

Table (2): Shows other obstetric outcomes.

	Mean ±SD
Mean time lapse from valve replacement to pregnancy in years	7.70±4.86
Mean pregnancy duration at delivery in weeks	36.08±3.82
Mean duration of abortion in weeks	10.66±3.26
Mean parity	1.06±1.10
Mean fetal weight at delivery in kg	2.62±0.38

Table (3): Shows ultrasound findings in the study group.

Fetal ultrasound findings	N=119	(100%)
Normal scan	70	58.8
IUGR	12	10.1
IUFD	9	7.6
Missed abortion	22	18.52
<i>Congenital anomaly:</i>		
Vactral syndrome	1	0.84
Dandy-walker syndrome	1	0.84
Ventriculomegally-cerebral hemorrhage	4	3.3

IUGR (intrauterine growth retardation), IUFD (intra uterine fetal death). By ultra sound there were 4 twin pregnancies. One of the twin pregnancies has intra uterine fetal death at 28 weeks of pregnancy, 3 twin's pregnancies were normal scan by ultrasound. The congenital anomalies diagnosed by ultrasound were as following; Vactral syndrome (hiatus hernia + omphalocele with herniated liver, bowel, heart (ectopiacordis) (acrania) diagnosed at 16 weeks of pregnancy, and one cases with Dandy-walker syndrome(ventriculomegaly + cerebral hemorrhage + hydrocephalus) diagnosed after 16 weeks of pregnancy and 4 cases with cerebral hemorrhage and ventriculomegally diagnosed after 30 weeks of pregnancy. The dose of warfarin was more than 5mg in the 6 pregnant women. There were 5 pregnant women used who used (warfarin) regimen throughout their pregnancy, and there was one pregnant woman used (heparin-warfarin-heparin) regimen throughout her pregnancy.

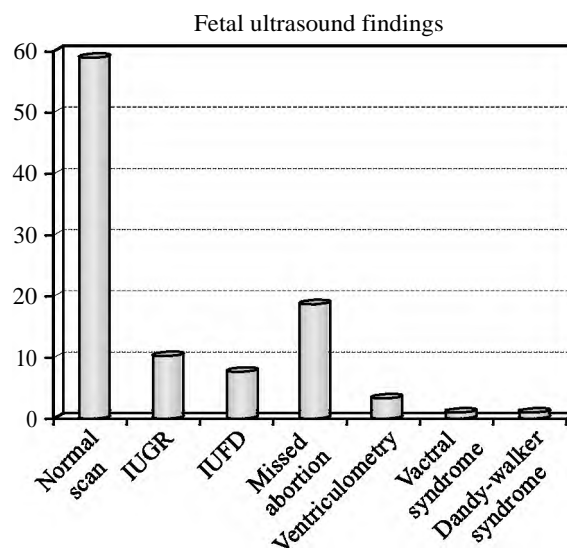


Fig. (1): Shows the fetal ultrasound findings in the study group.

Table (4): Shows pregnancy outcomes in the study group.

Pregnancy outcomes	N=119	(100%)
Live birth rate	82	68.9
Full term babies	57	47.9
Low birth weight (LBW)	12	10
Preterm delivery	13	11
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Total abortions	24	20.1
Therapeutic	2	1.6
Missed	22	18.5
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Neonatal death	4	3.4
IUFD (Still birth)	9	7.6

Therapeutic abortion was done to 2 cases due to congenital anomalies of the babies diagnosed by 3D ultrasound, first case was vactral syndrome (omphalocele with very wide defect herniated liver, bowel and heart (ectopiacordis), acrania) incompatible with life so therapeutic abortion was done at 4 months and 5 days and she was on warfarin more than 5mg with INR (2.5). Second case was Dandy-walker syndrome (ventoculomegally dilated cysterna magna, limited limb movements (warfarin embryopathy) incompatible with life, therapeutic abortion was done at 4 months 3 days she was on warfarin more than 5mg with INR (2.45). There were two pregnant women with twin pregnancies delivered preterm (32-33 weeks of pregnancy) and their children admitted to the neonatal intensive care unit also, one pregnant woman with twin pregnancy with IUFD (at 28 weeks of pregnancy) and another woman with twin pregnancy delivered by caesarian section near full term and her babies were good.

There were four cases with congenital anomalies of the babies occurred after the second trimester (after 30 weeks of pregnancy) with the following findings: (ventriculomegally, cerebral hemorrhage) three of them occurred with warfarin taking through

their pregnancy and one cases occurred with (heparin warfarin heparin) and warfarin doses was more than 5mg; for medico legal aspect and religious aspect they did not choose to terminate their pregnancy. Planned caesarian section delivery was done to at 33-34 weeks of gestation followed by neonatal death of the four cases.

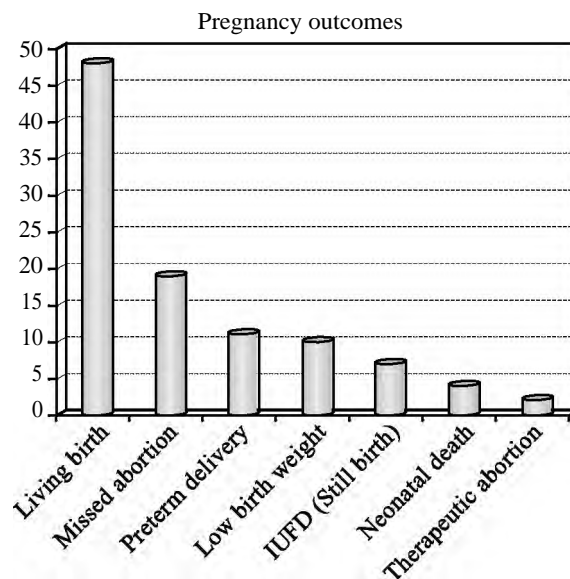


Fig. (2): Shows pregnancy outcomes in the study group.

**Relations:**

Table (5): Shows relation between fetal ultrasound images 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)		
<b>Fetal U/S images:</b>					
<i>Normal scan:</i>					
N	50	13	7	70	0.006*
%	70.4%	46.4%	35.0%	58.8%	
<i>IUGR:</i>					
N	9	0	3	12	0.122
%	12.7%	0%	15.0%	10.1%	
<i>IUFD:</i>					
N	7	0	2	9	0.229
%	9.9%	0%	10.0%	7.6%	
<i>Missed Abortion:</i>					
N	4	10	8	22	0.001 *
%	5.6%	35.7%	40.0%	18.5%	
<i>Congenital anomaly:</i>					
N	1	5	0	6	0.002*
%	1.4%	17.9%	.0%	5%	

There is statistical significance between normal scans diagnosed by fetal ultrasound and regimen of anticoagulation, normal scans were higher with (heparin-warfarin-heparin) regimen (50/71) (70.4%) with significant *p*-value (0.006). There is statistical significance between missed abortions and regimen of anticoagulation, missed abortions were higher with heparin (40%) and warfarin (35.7%) least with heparin-warfarin-heparin (5.6%) with signif-

icant *p*-value (0.001). There is also statistical significance between regimen of anticoagulation and fetal congenital anomaly, which was higher with (warfarin) (17.9%) with significant *p*-value (0.002). IUGR was higher with (heparin) (3/20) (15%). IUFD was higher with (heparin-warfarin-heparin) (7/71) (9.9%). IUGR and IUFD were absent with (warfarin), *p*-value (NS).

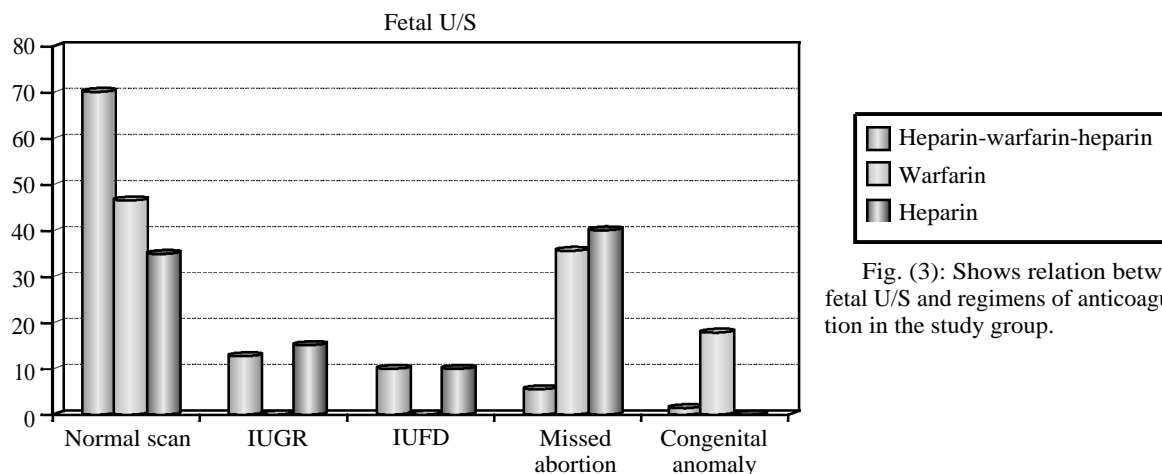


Fig. (3): Shows relation between fetal U/S and regimens of anticoagulation in the study group.

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

	Regimen of anticoagulation			Total n=119 (100%)	<i>p</i> - value
	Heparin-warfarin- Heparin (71)	Warfarin (28)	Heparin (20)		
<b>Pregnancy outcomes:</b>					
<i>Living birth rate:</i>					
N	59	13	10	82	0.002*
%	83%	46.4%	50%	69%	
<i>Full term:</i>					
N	47	6	4	57	0.001 *
%	66.2%	21.4%	20%	47.9%	
<i>Preterm:</i>					
N	3	7	3	13	0.009*
%	4.2%	25%	15%	10.9%	
<i>LBW:</i>					
N	9	0	3	12	0.122
%	12.7%	0%	15%	10.1%	
<i>Fetal loss rate:</i>					
N	12	15	10	37	0.002*
%	17%	53.6%	50%	31%	
<i>IUFD:</i>					
N	7	0	2	9	0.229
%	9.9%	0%	10%	7.6%	
<i>Abortion:</i>					
N	4	12	8	24	0.001 *
%	5.6%	42.9%	40%	20.2%	
<i>Neonatal death:</i>					
N	1	3	0	4	0.045 *
%	1.4%	10.7%	0%	3.3%	

The total number of live births in the study group was (82/119) (69%). There is statistical significance between regimens of anticoagulation and live birth in the study group, in this study live births were higher with heparin-warfarin-heparin (59/71) (83%) lower with heparin (10/20) (50%) and least with warfarin (13/28) (46.4) with significant *p*-value (0.002). There is statistical significance between regimens of anticoagulation and the fetal loss rate which was higher with warfarin (15/28) (53.6%) and heparin (10/20) (50%) and least with heparin-warfarin-heparin (12/71) (17%) with significant *p*-value (0.002). There is statistical significance between regimens of anticoagulation and healthy babies were higher with (heparin-warfarin-heparin) (47/71) (66.2%) with significant *p*-value (0.001). Also there is statistical significance between regimens of anticoagulation and preterm delivery, which was higher with (warfarin) (7/28) (25%), lesser with (heparin) (4/20) (20%), and least with (heparin-warfarin-heparin) (3/71) (4.2%) with significant *p*-value (0.009). There is statistical significance between regimens of anticoagulation and abortion, which was higher with (warfarin) (12/28) (42.9%), lesser with heparin (8/20) (40%) and least with (heparin-warfarin-heparin) (4/71) (5.3%), with significant *p*-value (0.001). There is statistical significance between regimens of anticoagulation and neonatal death which was higher with (warfarin) (3/28) (10.7%), lower with (heparin-warfarin-heparin) (1/71) (1.4%) and absent with (heparin) with significant *p*-value (0.045). IUFD was higher with (heparin-warfarin-heparin) (7/71) (9.9%) and lower with (heparin) (2/20) (10%) and LBW was higher with (heparin) (3/20) (15%), lower with (heparin-warfarin-heparin) *p*-value (NS).

There were 28 cases taken warfarin throughout their pregnancy and 71 cases used warfarin with heparin through their pregnancy. There is statistical significance between fetal outcomes and warfarin doses. Fetal outcomes were good with warfarin doses  $\leq 5$  (72.2%) with significant *p*-value 0.001. Preterm deliveries were higher (7/56) (12.5%) with warfarin  $>5$ mg. IUFDs were higher (6/56) (10.7%) with warfarin  $>5$ mg. Abortions were higher (12/56) (21.4%) with warfarin  $>5$ mg. LBWs were higher (4/43) (9.3%) with warfarin  $\leq 5$ mg. Neonatal deaths were higher with warfarin  $>5$ mg (4/56) (7.2%), *p*-value (NS).

Pregnancy outcomes of 119 pregnancies were as following, (57/119) resulted in healthy babies, which were higher with (heparin-warfarin-heparin) (47/71) (66.2%). The total live births were higher with (heparin-warfarin-heparin) (59/71) (83%),

lower with heparin (10/20) (50%) and least with warfarin (13/28) (46.4%).

Fetal complications occurred in (62) cases (52.1%) and were due to the following causes: Spontaneous abortion (22/119) (18.5%), therapeutic abortion (2/119) (1.6%) due to congenital anomalies, intrauterine fetal death IUFD (9/119) (7.6%), neonatal death (4/119) (3.4%) due to congenital anomalies, preterm delivery babies were (13/119) (11%) and low birth weight babies were (12/119) (10%).

Table (7): Shows relation between warfarin doses and fetal outcome in the study group.

(Warfarin dose range) (3-12mg)	Warfarin doses In mg		Total n=99 (100%)	<i>p</i> -value
	$>5$	$\leq 5$		
	56	43		
Fetal outcome:				
Good:				
N	22	31	53	0.001*
%	39.3%	72.2%	53.5%	
Preterm Delivery:				
N	7	3	10	0.366
%	12.5%	6.9%	10.1%	
IUFD:				
N	6	1	7	0.107
%	10.7%	2.3%	7.1%	
Abortion:				
N	12	4	16	0.104
%	21.4%	9.3%	16.2%	
LBW:				
N	5	4	9	0.949
%	8.9%	9.3%	9.1%	
Neonatal death:				
N	4	0	4	0.074
%	7.2%	0%	4%	

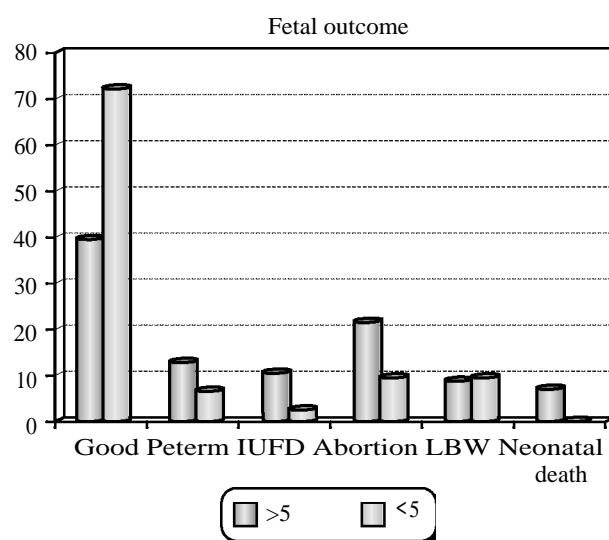


Fig. (4): Shows relation between warfarin doses and fetal outcomes in the study group.

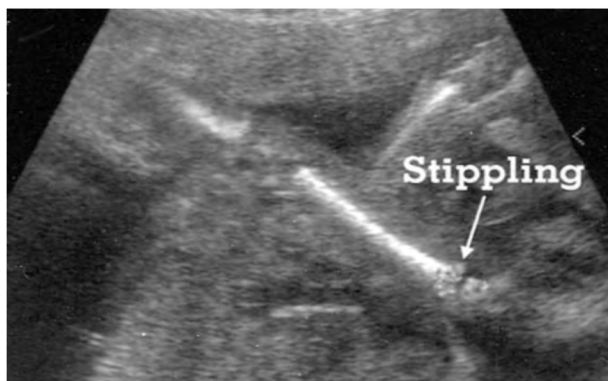


Fig. (5): Shows stippling of head of femur (5).



Fig. (6): Shows Trans axial view of skull shows bilateral ventriculomegaly (5).



Fig. (7): Post mortem fetal picture of warfarin embryopathy (5).

### Discussion

Pregnant women in 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 [6].

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 [7].

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 [3].

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 [4].

Revising the obstetric outcomes in the current study the mean pregnancy duration at time of delivery was  $(36.08 \pm 3.82)$  week, Mean duration of abortion was  $(10.66 \pm 3.26)$  week. Mean time lapse from valve replacement to pregnancy in years was  $(7.70 \pm 4.86)$ .

Mean fetal birth weight at delivery in this study was low  $(2.62 \pm 0.38)$  kg, and the range  $(1.8-3.5)$  kg. This comes in accordance to a study done by Pinhas [8] they found, the mean fetal birth weight was low  $(2.54 \pm 0.98)$  kg in women with prosthetic metallic heart valve but comes in difference to a study done by Niloufar [9] the mean weight of the newborns was  $2784.3 \pm 579.3$  gram.

As regard the relation between fetal ultrasound images and the regimen of anticoagulation in the study group. In this study, normal scans diagnosed by fetal ultrasound normal scans were higher with (heparin-warfarin-heparin) regimen  $(50/71)$  (70.4%) with significant  $p$ -value (0.006).

Missed abortions were higher with (heparin) (40%) and warfarin (35.7%) least with heparin-warfarin-heparin (5.6%) with significant  $p$ -value (0.001). The fetal congenital anomalies were higher  $(5/28)$  (17.9%) with (warfarin) with significant  $p$ -value (0.001) this comes in accordance to a study done by Zienab [10] in which they found that, congenital anomaly was higher  $(3/34)$  (8.8%), with (warfarin) and also comes in accordance to a study done by (chan) [11] in which they found that the use of OA (oral anticoagulation) throughout pregnancy is associated with warfarin embryopathy in (6.4%) but comes in difference to a study done by



Niloufar [9] there was no case of embryopathy in the study.

IUGR was higher with (heparin) (3/20) (15%). IUFD was higher with (heparin-warfarin-heparin) (7/71) (9.9%). IUGR and IUFD were absent with (warfarin),  $p$ -value (NS).

In this study preterm delivery was statistically higher with (warfarin) (7/28) (25%), lesser with (heparin) (3/20) (15%), and least with (heparin-warfarin-heparin) (3/71) (4.2%) with significant  $p$ -value (0.001), this comes in accordance with a study done by Eulogio [12], in which they found The incidences of preterm delivery was significantly higher (50%) with warfarin.

In this study abortion was statistically higher with (warfarin) (12/28) (42.9%) and heparin (8/20) (40%) and least in with (heparin-warfarin-heparin) (4/71) (5.6%) with significant  $p$ -value (0.001) this comes in accordance to a study done by (Geelani) [13] reported a similar incidence of abortion in warfarin and heparin groups, but comes in difference to a study done by Salazar [14] higher abortion was high with warfarin only (37.5%) and Shannon [15] who reported high rate of abortion with warfarin only (37%), and in difference with Akhtar [16] study, spontaneous abortion occurred more frequently in the heparin group only.

As regard neonatal death, in this study neonatal death was higher with (warfarin) (3/28) (10.7%), lower with (heparin-warfarin-heparin) (1/71) (1.4%) and absent with (heparin) with significant  $p$ -value (0.045), this comes in accordance with a study done by Eulogio [12] in which they found neonatal deaths (5/40) (12.5%) were higher with (warfarin), ( $p$ =NS).

In this study IUFD was higher with (heparin-warfarin-heparin) (7/71) (9.9%) and lower with (heparin) (2/20) (10%), and absent with (warfarin). LBW was higher with (heparin) (3/20) (15%), lower with (heparin-warfarin-heparin) (9/71) (12.7%) and absent with (warfarin),  $p$ -value (NS), this comes in difference with Eulogio [12] in which they found, low birth weight were significantly higher (46.6%) with (warfarin) (10.5%) than with (heparin), with significant ( $p$ <0.05).

As regard the relation between fetal outcome and regimen of anticoagulation in the study group. In this study live births with was higher (heparin warfarin heparin) (59/71) (83%), lower with both heparin (10/20) (50%) and with warfarin (13/28) (46.4%) with significant  $p$ -value (0.002). Full term babies were higher with (heparin-warfarin-heparin)

(47/71) (66.2%), least with (warfarin) (6/28) (21.4%), and with (heparin) (4/20) (20%), with significant  $p$ -value (0.001), so there is no difference as regard the fetal outcome between the two regimens heparin or warfarin alone, this comes in accordance to a study done by (Sadler) [14], pregnancy loss rate was 70% in pregnancies treated with warfarin, compared with 25% for those used (heparin warfarin heparin), and comes in accordance to a study done by Judith [17], 418 reported pregnancies in which warfarin was used, two-thirds of the fetal outcome were normal infants. In 135 pregnant women used heparin, two-thirds of fetal outcome were normal, in their study they concluded that heparin does not appear to be a clearly superior alternative to warfarin for better fetal outcome and indifference to a study done by Niloufar [9], in group I (warfarin), there were (60.5%) live births, (34%) abortions (2.3%) stillbirth. In group II (heparin-warfarin-heparin), there were (60%) live births, (30%) abortions, and (11%) stillbirth. There were no significant differences with respect to the fetal outcome between the two groups and in difference with a study done by Zienab [10] healthy babies were higher with (heparin) (38/66) (57.6%) than with (warfarin) (18/34) (52.9%), ( $p$ =NS), and also in difference with a study done by Amir [18] healthy babies were higher with (heparin) (7/11) (63.6%), lower with (warfarin) (22/49) (57.9%), ( $p$ =NS).

As regard the relation between fetal outcome and warfarin doses in the study group. In this study fetal outcomes were good with warfarin doses  $\leq 5$  (72.2%) with significant  $p$ -value 0.001. Preterm deliveries were higher (7/56) (12.5%) with warfarin  $>5$ mg. IUFDs were higher (6/56) (10.7%) with warfarin  $>5$ mg. Abortions were higher (12/56) (21.4%) with warfarin  $>5$ mg. LBWs were higher (4/43) (9.3%) with warfarin  $\leq 5$ mg. Neonatal deaths were higher with warfarin  $>5$ mg (4/56) (7.2%),  $p$ -value (NS), this comes in accordance with Akhtar [16] study, the risk is probably lower if the dose  $\leq 5$ mg of Warfarin is prescribed, and also comes in accordance with a study done by Vitale [19]. Patients used warfarin doses during pregnancy  $>5$ mg had (22/58) (38%) had higher fetal complications, whereas those taking a dose  $\leq 5$ mg had lesser (5/58) (8.6%) fetal complications ( $p=0.0001$ ) and also in accordance to a study done by Cotrufo [2], pregnancy loss occurred in (23/71) (32.4%) of pregnancies with warfarin daily dosage over 5mg per day and was a significant predictor of poor pregnancy outcome ( $p$ <.001). And also in accordance to a study done by Niloufar [9], our previous study confirmed that a low dose of warfarin during pregnancy is almost safe.

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## اختيارات موانع التجلط فى الأمهات اللائى لديهن صمام معدنى صناعى بالقلب وفتائج ذلك على الجنين

يعتبر استخدام المواد المانعة للتجلط ضرورى للحوامل اللائى لديهن صمام معدنى صناعى بالقلب وذلك لمنع تجلط الدم نتيجة اصطدائه بالصمام الصناعى والذى قد يسبب الوفاة للام نتيجة الجلطات على القلب وفى هذا البحث نتطرق إلى اثار بعض الأدوية المانعة لتجلط على الجنين.

المرضى : أجريت الدراسة على السيدات الحوامل اللائى لديهن صمام صناعى معدنى أو أكثر بالقلب. وقد أجريت الدراسة على عدد ١١٩ حالة حمل لعدد ١١٢ سيدة بداية من شهر يناير ٢٠١٣ إلى نهاية ديسمبر ٢٠١٥.

وأساليب البحث : بالنسبة لجمع المرضى تم عمل الآتى :

الحصول على الاستشارة الطبية اللازمة لاختيار طريقة العلاج بمانع التجلط على صمام 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 (الماريقان) أثناء المرحلة الأولى للحمل إلى نهاية المرحلة الأخيرة للحمل مع إيقافه فى الأسبوعين الأخيرين للحمل أو مع حدوث الام المخاض والولادة.

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

٣- عقار الهيبارين من بداية المرحلة الأولى للحمل والاسبوعين الأخيرين للحمل ما قبل الولادة، واستخدام عقار الوارفارين (الماريقان) فى الفترة التى بينهما.

وقد تم عمل الفحوصات الآتية :

وبالنسبة للاشعات التشخيصية : تم عمل أشعة تليفزيونية على القلب من بداية الحمل، وحسب الاحتياج بعد فحص القلب وفى الشهر التاسع للحمل للحالات التى أكتمل 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 الأسبوع العشرين إلى الأسبوع الرابع والعشرين لكل الحالات التى وصل عمر الجنين لها لهذه المرحلة وخصوصاً الحالات التى أخذت عقار الوارفارين (الماريقان) كمانع للتجلط على الصمام الصناعى مع الحمل وذلك لتحديد أى تشوهات وخصوصاً التى قد تحدث بسبب تعاطى عقار الوارفارين.

والغرض الأساسى من البحث هو : متابعة الجنين من حيث النمو ورصد حدوث أى مضاعفات للجنين مثل التأخر فى نمو الجنين، حدوث التشوهات أو الاجهاض أو الولادة المبكرة، أو وفاة الجنين قبل أو أثناء الولادة.

الغرض الثانوى : معرفة الجرعة المناسبة من عقار الوارفارين (الماريقان) والتى تمنع التجلط على الصمام ولا تحدث تشوه للجنين أو مضاعفات للحمل.