Pregnancy Outcome in Women with Prosthetic Valve in Qena University Hospitals

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Abstract

Background: The combinations between heart disorders and gestation could be challenging to the physician managing the mother and fetus together. Gestation afterward mechanical heart valve replacements require critical coagulation controlling. Specific consideration must be given to the incidence of complications throughout anti-coagulation treatment.

Objectives: was to evaluate the outcome of the antenatal, natal and postnatal outcome of women with prosthetic valve with pregnancy according to the local policies and protocols in our department.

Patients and methods: This study was a cohort one that was demonstrated at Obstetrics and Gynecology Department, Qena Faculty of medicine, South Valley University in the period between July 2019 to 30th of June 2020.

Results: The results of current study showed a positive correlation between dose of warfarin and neonatal outcome as in group A (64% with good outcome , 11.8% misscarige) compared with group B (22.2% with good outcome 38.9% misscarige), and good fetal / neonatal outcome was observed in(42.9%)of cases. The miscariage rate was (25.7%). Congenital anomaly was seen in (8.6%). Furthermore, (22.9%) of pregnancies ended as IUFD.

Conclusion: Warfarin as an anticoagulant for pregnant women with prosthetic valve throghout pregnancy seems to be secure for the mothers due to a lesser occurrence of thromboembolic conditions than un-fractionated or lower-molecular-weight heparin. The fetal / neonatal outcome is good especially if doses not exceed 5mg.

Keywords: Prosthetic thrombosis; Anti-coagulation; Neonatal outcome; Congenital anomaly

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Introduction

With the current developments in the surgical treatments of valvular heart diseases, increasing number of women present to the obestetricans with prosthetic valve during pregnancy. **(Marijon et al., 2017)**

Prosthetic thrombosis is an extraordinary complication; however, it has excessive death and morbidity. Young females of child-bearing age which have prosthetic heart valves are at elevated danger of thrombosis throughout pregnancy because of alterations in coagulation factors. (Nishimura et al., 2014)

In Arab Republic of Egypt, this issue is of special consideration, as big number of females within child-bearing age have prosthetic valves due to the fact that rheumatic fever and concomitant valvular heart disorder are still frequent in Egypt. (Zeinab et al., 2008)

Mechanical heart valves have excessive hazards of thrombosis and thromboembolism with out concomitant anti-coagulation. The hazards are additionally elevated if there's atrial fibrillation or if the valve is one of the old models, specially withinside the mitral location. Gestation rises the hazard of thromboembolic disorder in addition to the hazard of anti-coagulation for mother and fetus in cases with mechanical valves. (Elkayam et al., 2015)

There are many challenges in the treatment of gravid ladies with prosthetic heart valves, gravid ladies are at danger of heart failure, thromboembolic complications, arrhythmia, infectious endocarditis and parental death. The hyper-coaguable state of pregnancy rises the thromboembolic danger and consequently the selection of anti-coagulant is specially essential in pregnancy. (McLintock et al., 2014)

This work aimed to assess the outcome of the antenatal, natal and postnatal outcome of women with prosthetic valve with pregnancy according to the local policies and protocols in our department.

Patients and methods

This study was a cohort one performed at Obstetrics and Gynecology dep., Qena Faculty of medicine, South Valley University in the period between July 2019 to 30th of June 2020.

Inclusion criteria

- This work was performed on Gravid females with prosthetic heart valve visiting the department of Obstetrics and Gynaecology, Qena Faculty of Medicine, South Valley University.

Exclusion criteria

- Pregnant woman with associated diseases in addition to prosthetic heart valve replacement.

Samples

- This work was conducted on pregnant women with prosthetic valve in Obstetric and Gynaecology department, South Valley University hospital.

Data was grouped into two parts:

1. Retrospective part from hospital records throughout the period of July 2018 till 30th June 2019.
2. Prospective cohort from women admitted to the Obstetrics and Gynaecology department throughout the period of the first of July 2019 to 30th of June 2020.

Study tools

I-History taking

II-Examination: General and local examination

III- Investigations:

1- Laboratory investigation:

Complete blood count, prothrombin time, prothrombin concentration and international normalised ratio (INR)

2- **2D Ultrasound:** Evaluate perinatal congenital anomalies, estimated fetal weight, estimated gestional age, amniotic fluid index and the placenta.

3- Echocardiography: Evaluate :

1- Ejection fraction.
2- State of cardiac valve.
3- Pulmonary arterial systolic pressure.

IV- Intervention:

According to the local protocol in South Valley University hospitals, all pregnant women receive warfarin from beginning of pregnancy till 36-wks of pregnancy. Females are shifted to therapeutic dose of enoxaparin from 36 weeks until normalization of INR then termination is done.

V- Delivery :

1- Stop LMWH 24 hours bfore induction of labor or CS.

2- Receive warfarin at 5 th day overlapped with LMWH.

3- Antibiotic cover against infective endocarditis in form of Amoxicillin &Gentamycin.

4- Evaluation of the cardiac status of the mother until the time of discharge from the hospital.

5- Evaluation the general condition of the fetus as regards:

- APGAR Score at 5&10 minutes.
- Fetal dysmorphic features especially facial and limb problems.
- Cardiac auscultaion.
- Reflexes to test integrity of CNS:

Research outcome measures

a. Primary (main):

1- Detect the thrombo-prophylactic capacity of Warfarin in gravid females with prosthetic valve.

2- Detect the fetal, perinatal, and postnatal effects of exposure to anti-coagulants including live births rate & congenital anomalies.

b. Secondary (subsidiary):

- Detect non-thrombotic complications including number of Cesearean Sections, heart valve dysfunction, infective endocarditis, bleeding complications, anemia, arrhythmia and death.

Ethical considerations: All patients signed a written Informed consent. The research conducted by scientifically qualified and trained personnel. The consent form provided with the proposal. The proposal will be reviewed by the committee of ethics at the Medicine Faculty.

Statistical analysis

The collected data was analysed via SPSS 21.0 (by IBM, Inc., Chicago, IL, USA).

Significance Testing: chi-square testing was employed to match the change in frequency distributions between various groups.

Continuous variables; in-dependent t-testing was done to match the mean of dichotomous data. A significance was taken in to consideration at p-value ≤0.05.

Results

Our study was a cohort study conducted on gravid females with prosthetic valve in the department of Obstetrics and Gynecology, South Valley University hospitals. All pregnant women received warfarin from beginning of pregnancy until 36 weeks of gestation. Women were be shifted to therapeutic dose of enoxaparin from 36 weeks until normalization of INR then termination was done. We divided them into 2 groups: **Group A**: receiving ≤5 mg of warfarin. **Group B**: receiving >5 mg of warfarin.

In this study we reviewed patient record of 50 cases with prosthetic valve during pregnancy, 10 records with associated other medical diseases were excluded. A further 5 cases excluded due to incomplete data. A total of 35 cases were included in final analysis.

(**Table.1**) shows that 48.6 % of women with prosthetic valve received a dose of warfarin ≤5 mg. Most of women have mitral valve replacement (82.9).

(**Table.2**) shows that good fetal / neonatal outcome was observed in (42.9%) of cases. The miscariage rate was (25.7%). Congenital anomaly was seen in (8.6%). Furthermore, (22.9%) of pregnancies ended as IUFD

(**Table.3**) shows: No statistical significant difference ($p>0.05$) among the studied groups regarding miscarriage, congenital anomaly & IUFD. Statistically significant difference ($p<0.05$) among the studied groups regarding good neonatal outcome.

(**Table. 4**) shows the maternal outcome in all studied patients. All studied patients had CS delivery with no valve dysfunction, valve thrombosis, bleeding complications or arrhythmia.

(**Table .5**) shows: No statistically significant change ($p>0.05$) among mitral & aortic valves as regard miscarriage, congenital anomaly & IUFD. Significant change ($p<0.05$) among mitral & aortic valves as regard good neonatal outcome

Table 1. Clinical data of participants

Variables	Frequency	Percent
Group A(Warfarin ≤5mg) B(Warfarin >5mg)	 17 18	 48.6% 51.4%
Age (in years)	32.7 ± 5.5	
Number of CS	1.7 ± 1.1	
BMI	23.9 ± 3.5	
Type of Prosthetic valve Mitral Aortic	 29 6	 82.9% 17.1%

Table 2. Fetal / neonatal outcome of all participants

Variables	Frequency	Percent
Miscarriage	9	25.7%
Good	15	42.9%
congenital anomaly	3	8.6%
IUFD	8	22.9%
Total	35	100%

Table 3. Relation between dose of Warfarin (mg) and fetal / neonatal outcome

Variables			Dose of warfarin		P value
			Group A ≤5	Group B >5	
Fetal / neonatal outcome	Miscarriage	Count	2	7	0.066 NS
		% within dose of warfarin	11.8%	38.9%	
	Good	Count	11	4	0.011 S
		% within dose of warfarin	64.7%	22.2%	
	Congenital anomaly	Count	2	1	0.511 NS
		% within dose of warfarin	11.8%	5.6%	
	IUFD	Count	2	6	0.128 NS
		% within dose of warfarin	11.8%	33.3%	
Total		Count	17	18	
		% within dose of warfarin	100.0%	100.0%	

Table 4. Maternal results in gravid females with prosthetic valve using warfarin throughout pregnancy

Variables		n	%
Mode of delivery	NVD	0	0%
	CS	35	100%
Valve dysfunction	No	35	100%
	Yes	0	0%
Valve thrombosis	No	35	100%
	Yes	0	0%
Bleeding complications	No	35	100%
	Yes	0	0%
Arrhythmia	No	35	100%
	Yes	0	0%

Table 5. Relation between type of prosthetic valve and fetal/ neonatal outcome

Variables			Type of prosthetic valve		P value
			Mitral (n = 29)	Aortic (n = 6)	
Neonatal outcome	Miscarriage	Count	8	1	0.465 NS
		% within type of prosthetic valve	27.6%	16.7%	
	Good	Count	10	5	0.027 S
		% within type of prosthetic valve	34.5%	83.3%	
	Congenital anomaly	Count	3	0	0.41 S
		% within type of prosthetic valve	10.3%	0.0%	
	IUFD	Count	8	0	0.143 NS
		% within type of prosthetic valve	27.6%	0%	

Discussion

The combinations between heart disorders and gestation could were challenging to the physician managing the mother and fetus together. Gestation afterward mechanical heart valve replacements require critical coagulation controlling. Specific consideration must be given to the incidence of complications throughout anti-coagulation treatment. **(Kawamata et al., 2016)**

This work involves 29-cases (82.9%) with mitral valve replacements (MVR), 6-cases(17.1%) with aortic valve replacements (AVR). A total of 18-cases (51.4 %) received greater than 5 mg of oral anti-coagulant (warfarin), 17-cases (48.6%) received lower than or equal 5 mg of warfarin, throughout the pregnancy.

In our study we found that all studied patients had CS without maternal complications as valve dysfunction, valve thrombosis, bleeding complications or arrhythmia in the two groups (Group A: receiving ≤5 mg of warfarin and Group B: receiving >5 mg of warfarin).

This agrees with findings of the study by **Lee et al., 2007** they reported that one in 25 gravid females with a mechanically prosthetic heart valve who are managed with oral anti-coagulants will progress valve thrombosis **(Lee et al., 2007)**. Also, the study in California (in 2005), thromboembolisms happened in 3.9% of 788 females with mechanically prosthetic heart valve who were managed with oral anti-coagulants throughout gestation **(Ufer et al., 2005)**. In comparison, **Quinn et al**., **2009** found that In the last short period, many studies showed the relation between use of Heparin and high complication and mortality rate **(Quinn et al., 2009)**. While Moher et al., had been reported that VKAs were suggested for females with MHVs in the 2nd and 3rd trimester and their usage in the 1st trimester was taken in to consideration if the everyday dosage needed to accomplish a therapeutic INR is lower than or equal 5mg. **(Moher et al., 2009)**

In current study, good fetal / neonatal outcome was observed in (42.9%) of cases. The miscariage rate was (25.7%). Congenital anomaly was seen in (8.6%), Furthermore, (22.9%) of pregnancies ended as IUFD. This goes in line with the result of the reserch done by Van Driel et al., In moms utilizing warfarin during gestation, the occurrence of skeletal anomalies was 6% in 394 liveborn kids. In the children of females who utilized heparin from the week-6 to -12 of gestation no skeletal anomalies were found. **(Van Driel et al., 2002)** Opposite to our findings, Salazar and colleagues have concluded a 37.5 % occurrence of unprompted abortions in a series of cases managed with subcutaneous heparin through the gestation 1st trimester. These high abortions can be clarified by placental hemorrhage, that can happen throughout operative anti-coagulation with Heparin. **(Salazar et al., 1996)**

The current work concluded a positive association among dose of warfarin and neonatal outcome as in group A (64% with good outcome, 11.8% misscarige) compared with group B (22.2% with

good outcome 38.9% misscarige). New data present unmatching result of whether or not a safe dosage of warfarin may present. In McLintock et al, concluded many new investigations that propose a dosage association might present for warfarin embryopathy, but unclear result can be concluded that warfarin embryopathy was dosage correlated. While a slight cases number were concluded, there were 5-cases of warfarin embryopathy in females who were taking less than or equal 5mg of warfarin and 7-cases in females who were using greater than 5mg every day **(McLintock et al., 2014)**. Although van Hagen et al, concluded a nonsignificant change in fetal loss or miscarriage among high-dosage warfarin (>5mg everyday) and low-dosage (≤5mg daily). **(Van Hagen et al., 2015)**

Although our study results showed that all pregnant women (35 patient) delivered by ceaserean section, And this is compatible with the study done by Lawley et al., they found that 16 women (34.7%) had a vaginal birth, with 30 (65.2%) having a lower segment caesarean sections (LSCS).

In current study showed nonsignificant changes among the two groups regarding women ages, body mass index or type of prosthetic valve (mitral or aortic).

Finally, there are many suggested protocols for the management of anticoagulation in females with prosthetic valave throughout gestation. Some authors use warfarin throughout pregnancy and subsitituting it with LMWH from the week-6 and week-12 because of neonatal complications then alternative coumarin derivatives limited number of weeks earlier to proposed birth. In our study we used established policy of use warfarin throughout pregnancy, we found that protocol has accepted outcome regarding maternal outcome. However, the fetal/neonatal outcome is not in favour with this protocol, especially in women who take a higher dose of warfarin.

Conclusion

Warfarin as an anticoagulant for pregnant women with prosthetic valve throughout pregnancy seems to be more-safe for the mom due to a low occurrence of thromboembolic conditions than un-fractionated or low-molecular-weight heparin. The fetal / neonatal outcome is good especially if doses not exceed 5mg.

Conflict of Interest

The authors of the study have no conflict of interest related to this publication.

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