

Outcomes in IVF Conceived Pregnancies Complicated with Hypertensive Disorders

Krasniqi MV¹, Daka Q²

Abstract

Introduction: Many studies have demonstrated an increased risk of obstetrical and neonatal complications after assisted reproductive techniques treatment compared to spontaneously conceived pregnancies. There are no data regarding these outcomes in Kosovo. The aim of our study was, to compare maternal, obstetric and neonatal parameters of *in-vitro* fertilization (IVF) conceived pregnancies complicated with hypertensive disorders (HD) versus uncomplicated spontaneous conceived pregnancies in Kosovo. **Material and Methods:** This observational study was undertaken at the Department of Gynaecology, University Clinical Centre of Kosova, during a two year period. A total of 104 pregnant women were included in the study. Maternal, obstetrical and neonatal parameters in both groups were assessed and compared. Statistical analysis was performed using SPSS 22.0 statistical software. **Results:** Women that conceived through IVF and had HD during pregnancy were older ($p=0.0001$), primipara ($p=0.007$), had multiple pregnancies ($p=0.0001$) and had worse obstetrical outcomes including cervix insufficiency ($p=0.0001$), premature rupture of membranes ($p=0.0001$), and delivery type ($p=0.003$) compared to women that conceived spontaneously. The only statistically significant differences in neonatal outcomes were in the Apgar1st ($p=0.012$) and Apgar5th ($p=0.004$) scores that were higher among babies born from mothers that conceived through IVF and had HD during pregnancy. **Conclusions:** Results of our study are in line with the results from other countries in regards to maternal demographic profile, except education level and employment, and obstetrical outcomes. However, there were no differences in regards to neonatal outcomes between the two groups of babies other than in the Apgar 1st and Apgar 5th scores.

Key words: Hypertensive disorders, IVF, Kosovo, Outcomes.

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Acknowledgements: We acknowledge Dr. Sanije Gashi for her contribution on statistical analysis.

Funding: Nil

Conflict of Interest: None

Permission from IRB: Yes

How to cite

Krasniqi MV, Daka Q. Outcomes in IVF Conceived Pregnancies Complicated with Hypertensive Disorders. J Nepal Paediatr Soc 2017;37(2):159-163.

doi: <http://dx.doi.org/10.3126/jnps.v37i2.16989>

Introduction

Since the introduction of the in-vitro fertilization (IVF) treatment, the success rate of the procedure has been increased and most of the pregnancies after IVF result in normal healthy outcomes. However, the risk for a number of obstetric and neonatal complications due to these treatments remains unknown. Many studies on this topic report

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for an increased risk of: hypertensive disorders (HD), preterm delivery, placental abruption, placenta previa.

C-section delivery, low and very low birth weight (LBW and VLBW), congenital malformations, and neonatal mortality compared to spontaneously conceived pregnancies^{1,2,3,4}. The association of these complications to IVF treatment procedures can be explained partly by the high rate of multiple pregnancies and advanced maternal age, but also by the impact of technique, culture systems and medications used for treatment^{5,6,7}.

On the other hand, HD during pregnancies (chronic hypertension; gestational hypertension; preeclampsia; eclampsia; or HELLP syndrome), the most common medical problems encountered in pregnancy, remain an important cause of maternal and fetal morbidity and mortality^{8,9,10,11}. Data from observational studies demonstrate that HD during pregnancies are also associated to an increased risk of: preterm delivery, placental abruption, C-section, LBW and VLBW, neonatal morbidities or mortality^{10,12,13,14}. Worldwide, several risk factors have been described to be associated to HD during pregnancy such as: family history for HD in pregnancy or previous HD in pregnancy, extremes of maternal age, nulliparity, obesity, diabetes, chronic hypertension, multiple pregnancies etc.¹⁵. Beside other risk factors, IVF treatment technology appears to be one of the most important risk factors for occurrence of HD during pregnancy^{16,17}.

Although there is a large body of literature that describes the effect of IVF treatment on HD during pregnancy and association of both IVF treatment and HD to adverse maternal and neonatal outcomes, little is done to assess these associations in the Republic of Kosovo. Therefore, the aim of our study was, was to compare maternal characteristics, obstetric and neonatal outcomes of IVF conceived pregnancies complicated with HD versus uncomplicated spontaneous conceived pregnancies in Kosovo.

Material and Methods

This observational comparative study was undertaken at the Department of Gynaecology, University Clinical Centre of Kosovaduring a two year period, from January 2014-December 2015. The study was approved by the institutional ethical committee and informed consent was taken from mothers.

A total of 104 pregnant women were included, 54 pregnant women that conceived through IVF procedures and had HD during pregnancy (Group I) and 80 pregnant women that conceived spontaneously and

had no HD during pregnancy (Group II). Diagnoses of HD in pregnant women were set based on the criteria of the National High Blood Pressure Education Program Working Group⁸.

Baseline maternal characteristics were collected by nurse and included: age, education, parity and multiple pregnancies. Gynaecologist collected obstetrical and neonatal outcomes data including: cervical cerclage, premature rupture of membranes (PROM), type of delivery, preterm birth, gestational age, neonatal birth weight and Apgar score.

Maternal, obstetrical and neonatal data of IVF conceived pregnancies complicated with HD were compared to uncomplicated spontaneously conceived pregnancies using chi-squared or Fisher's exact tests for categorical variables and students t-tests for continuous variables. Categorical variables were expressed as percentages and continuous variables were expressed as mean \pm SD (median). Statistical analysis was performed using *SPSS 22.0* statistical software. Statistical significance was indicated by a *p* value < 0.05, whereas values of *p*<0.001 were considered as highly significant.

Results

A total of 104 pregnant women and 157 children were included in our data analysis. The detailed description of maternal demographic profile is presented in Table 1. Pregnant women that conceived through IVF treatment technology and had HD during pregnancy were older compared to women that conceived spontaneously and had no HD during pregnancy (39.7 \pm 7.8 years vs. 32 \pm 5.9 years) and this difference was highly statistically significant (*p*=0.0001). The majority of women in both groups were housewives (74%) and no difference, in between the two groups, was found in regard to working conditions. In regard to parity and multiple pregnancies, the difference in between the two groups was highly statistically significant. Primipara were 87% of women that conceived through IVF treatment technology and had HD during pregnancy compared to 67.5 % of women that conceived spontaneously and had no HD during pregnancy (*p*=0.007). Whereas, 42.6% of women in the IVF group delivered twins or other multiples compared to 2.5% of women that conceived spontaneously (*p*=0.0001).

Obstetrical and neonatal outcomes of the study population are presented in Table 2. Women that conceived through IVF treatment technology and had HD during pregnancy showed statistically significantly more frequent pregnancy complications in regard to cervix insufficiency, premature rupture of membranes and

Table 1: Maternal demographic profile

Maternal characteristics	Group I 54 (40.3%)	Group II 80 (59.7%)	p-value
Age	39.7±7.8 (SD)	32.0±5.9 (SD)	p=0.0001**
Work			
Housewife	40 (74.1%)	67 (83.8%)	p=0.250
Worker	14 (25.9%)	12 (15.0%)	
Student	/	1 (1.3%)	
Parity			
I	47 (87.0%)	54 (67.5%)	p=0.007**
II	2 (3.7%)	19 (23.8%)	
III+	5 (9.3%)	7 (8.8%)	
Multiple pregnancies			
I	31 (57.4%)	78 (97.5%)	p=0.0001**
II	22(40.7%)	2(2.5%)	
III+	1(1.9%)	/	

Group I = women that conceived through IVF procedures and had hypertensive complications during pregnancy. Group II = women that conceived spontaneously and had no hypertensive complications during pregnancy. PROM=Premature Rupture of Membranes. Data are presented as the Mean ± SD and as N (%). Values of p <0.05* were considered significant and p<0.001**as highly significant.

Table 2: Obstetrical and neonatal outcomes of study population

OBSTETRICAL OUTCOMES	Group I 54 (40.3%)	Group II 80 (59.7%)	p-value
Cervix insufficiency	8 (14.8%)	0 (0%)	p= 0.0001*
PROM	4 (7.4%)	0 (0%)	p= 0.0001*
C-section delivery	50 (92.6%)	53 (66.3%)	p=0.003*
NEONATAL OUTCOMES	75	82	
Gender			
Male	35 (46.7%)	45 (54.9%)	p=0.385
Female	40 (53.3%)	37(45.1%)	
Mean Gestational Age	36.1±2.2 (SD)	35.9±3.6 (SD)	p=0.716
Preterm births	29 (53.7%)	35 (43.8%)	p=0.339
Birth weight	2644±722.7 (SD)	2730±1014.3 (SD)	p=0.054
Apgar score			
Minute 1	7.0 ±1.7(SD)	6.2 ±2.2(SD)	p=0.012*
Minute 5	8.4 ±0.8(SD)	7.9 (0.9) ±0.9 (SD)	p=0.004*

Group I = women that conceived through IVF procedures and had hypertensive complications during pregnancy. Group II = women that conceived spontaneously and had no hypertensive complications during pregnancy. PROM=Premature Rupture of Membranes. Data are presented as the Mean ± SD and as N (%). Values of p <0.05* were considered significant and p<0.001**as highly significant.

delivery type. Cervix insufficiency and premature rupture of membranes were not noted in between uncomplicated spontaneously conceived pregnancies in compare to IVF conceived pregnancies that were complicated with HD during pregnancy where cervix insufficient occurred in 14.8% of cases and premature rupture of membranes in 7.4% of cases, therefore there was a highly statistical significance in between the two groups (p=0.0001). The percentage of women that delivered by C-section was 92.6% in the IVF group compared to 66.3% in the group that conceived spontaneously (p=0.003). Although, the

percentage of women that delivered preterm was higher in the group that conceived through IVF technology and had HD during pregnancy (56.3%), the difference with the group that conceived spontaneously (46.3%) was not statistically significant (p=0.339). Women that conceived through IVF procedures and had HD during pregnancy delivered 75 (35 F/40 M) infants, whereas those that conceived spontaneously and had no HD during pregnancy delivered 82 (45F/37M) infants. There was no difference when compared for infants' gender in between the two groups (p=0.385). We also found

that there was no statistical difference between the two groups of babies when compared for gestational age and birth weight. Mean gestational age of babies born from mothers that conceived through IVF technology was 36.1 ± 2.2 weeks compared to babies that were born from mothers that conceived spontaneously 35.9 ± 3.6 weeks ($p=0.716$), whereas mean birth weight of babies born from mothers that conceived through IVF technology and had HD during pregnancy was 26440 ± 722.7 g compared to babies that were born from mothers that conceived spontaneously 2730 ± 1014.3 g ($p=0.054$). Mean Apgar 1st and Apgar 5th indices were significantly higher within the babies born from mothers that conceived through IVF technology and had HD during pregnancy.

Mean Apgar 1st and Apgar 5th scores of babies born from mothers that conceived through IVF procedures were 7.0 ± 1.7 and 8.4 ± 0.8 scores, respectively compared to those of babies born from mothers that conceived spontaneously that had a mean Apgar 1st of 6.2 ± 2.2 scores and mean Apgar 5th of 7.9 ± 0.9 scores (Apgar 1st $p=0.012$, Apgar 5th $p=0.004$).

Discussion

According to the WHO, infertility and sterility will be the third-most serious disease worldwide in the 21st century, and the practice of IVF treatment will be increased¹⁸. On the other hand, HD remains the most common medical problem encountered during pregnancy that tends to increase more due to recent changes in the antenatal population¹⁰. The increasing use of IVF technology for infertility treatment and increased tendency for occurrence of HD during pregnancy due to this treatment, makes their obstetric and neonatal outcome aspects an important public health concern¹⁹. However, despite the worldwide spread of the problem, data from studies remain controversial due to differences in study designs, populations and countries. Although, Kosovo, a post-conflict country, has the youngest population in Europe, the growth rate of its population started to slow, and the birth rate is reduced as a consequence of the increased rate of infertility²⁰. Due to specific social and cultural characteristics of the Kosovo society to maintain a family structure we assume that, with this trend of infertility, the number of women that conceive through IVF procedures will be increased. To the best of our knowledge, this is the first study to investigate the maternal, obstetric and neonatal characteristics of IVF conceived pregnancies complicated with HD versus uncomplicated spontaneous conceived pregnancies in Kosovo. Data from this study will help determine the size and burden of the problem and serve to develop specific national prevention measure for HD in IVF conceived pregnancies.

Our analysis was carried out on 54 cases and 80 controls. In line with the results from other countries, women that conceived through IVF technology treatment and had HD during pregnancy were older ($p=0.0001$), primipara ($p=0.007$) and had multiple pregnancies ($p=0.0001$) compared to women that conceived spontaneously and had no HD during pregnancy, however, we found no difference in between the two groups of pregnant women in regard to education level and employment as the majority of pregnant women in both groups were housewives^{15, 16, 17, 19}.

Obstetrical and neonatal outcomes of the group that conceived through IVF technology treatment and had HD during pregnancy compared to those of the group that conceived spontaneously and had no HD during pregnancy varied. Women that conceived through IVF treatment technology and had HD during pregnancy showed statistically significantly more frequent pregnancy complications in regard to cervix insufficiency ($p=0.0001$), premature rupture of membranes ($p=0.0001$), and delivery type ($p=0.003$) in compare to women that conceived spontaneously. However, we found moderate differences in neonatal outcomes of babies born from the two groups of mothers. Although babies born from mothers that conceived through IVF technology and had HD during pregnancy had lower birth weight (86g); longer gestational age (0.2 weeks) and were born preterm (10%) in compare to those born from mothers that conceived spontaneously, this difference was not statistically significant. The differences in between the two groups of babies were highly statistically significant only for the Apgar 1st and Apgar 5th scores. Mean Apgar 1st and Apgar 5th scores of babies born from mothers that conceived through IVF technology were 7.0 and 8.4 respectively compared to those of babies born from mothers that conceived spontaneously 6.2 for Apgar 1 and 7.9 for Apgar 5 ($p=0.012$ and $p=0.004$, respectively).

Conclusion

The results of our study are in line with the results from other countries in regard to maternal demographic profile, beside education level and employment, and obstetrical outcomes. Obstetrical outcomes of women that conceived through IVF treatment technology and had HD during pregnancy were worse compared to those of women that conceived spontaneously.

Limitations

Our results could be a prone to several limitations due to the study design. Large cohort prospective studies, controlled for confounders, are necessary to confirm our findings.

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