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Research Article

Impact of Assisted Reproductive Technology on Embryonic Health Screening Tests: A Case-Control Study

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Abstract

Background: More than one million children throughout the world are born by using fertility techniques. In this process, human intervention and laboratory conditions may have an impact on the growth and development of the fetus.

Objectives: This study aimed at considering the effect of assisted reproductive techniques on the results of embryonic health screening tests.

Methods: In this case-control study, through the simple random sampling, 200 pregnant women who have used assisted reproductive techniques as a case group, and 200 natural pregnant women as a control group, were selected among clients referring to the Infertility Center of the Ome Leila hospital in Bandar Abbas province. By using an interview with pregnant women and investigating the embryonic screening tests, checklists were filled out and data analyzed by the SPSS version 21 and chi-square test.

Results: The majority of participating women in the study were housewives and had preliminary infertility. The body mass index (BMI) of most of them was normal. There was no significant difference between the final results of the embryonic screening test in the two groups at the first trimester ($P > 0.05$). However, In the second trimester, there was a significant difference between them. The positive results were higher in the case group in comparison with the control group ($P = 0.001$). The mean of all types of screening tests in the first trimester in both groups was not different, significantly ($P < 0.05$) although in the second trimester, the mean of all the tests including beta human chorionic gonadotropin (β-hCG) ($P = 0.006$) and *alpha-fetoprotein* (AFP) ($P = 0.018$) in both case and control groups, was significantly different. The mean of β-hCG and AFP was higher in the case group, while the mean of Estradiol and Inhibin, NB, and NT did not have any difference between them ($P < 0.05$).

Conclusion: Our study showed that embryonic screening tests, especially the β-hCG and AFP tests, would be affected by applying assisted reproductive techniques. For couples who had a history of infertility and used assisted reproductive methods, screening tests are essential in the first and second trimester.

Keywords: Pregnant women, Screening, Embryo, Infertility

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Background

Recent scientific has revolutionized the possibility of fertility for infertile couples. More than one million children worldwide are born using assisted fertility techniques. In this process, human intervention and laboratory conditions may affect the growth and development of the fetus (1,2), early diagnosis of a congenital anomaly at the beginning of pregnancy and termination of them can have a decline in the birth of disabled infants (1). Since congenital anomalies such as trisomy 13, 18, and 21 result in economic, social, and cultural burdens for families and society, so early diagnosis in the first trimester of pregnancy and termination can prevent these disadvantages. Down syndrome -in most cases- is a non-hereditary genetic condition (2,3). Prenatal screening tests are done to check and diagnose these three disorders (4,5). Embryonic health screening tests can be fulfilled from the beginning of the 11th week up to 13 week + 6 days. All people under 35 years old and over are advised to be screened. The stages include:

1. Providing history and conducting genetic council before examinations.
2. Performing ultrasound for measuring the nuchal translucency (NT) in the first trimester.
3. Measuring the pregnancy-associated plasma protein-A (PAPP-A) and human chorionic gonadotropin (hCG) in the maternal serum.
4. Assessment of the risk ratio by using software that is

approved by the Fetal Medicine Foundation (FMF).
5. Genetic council after examinations to interpret and justify the results and provide the necessary information and answer questions (4-6).

Screening for the second trimester is conducted between the 15th and 20th weeks of pregnancy and includes:
1. Measuring the NT and the nasal bone.
2. Measuring three biochemical markers in the mother's serum (*alpha-fetoprotein* [AFP], free β-hCG, and non-conjugated estradiol)
3. Also, in some laboratories, the fourth biochemical marker so-called Inhibin A is measured. This method is nominated quadruple test that determines whether the baby is at risk for certain chromosomal disorders and neural tube defects or not)6).

Several studies showed that children who are born via fertility treatment, especially In vitro fertilization (*IVF*), have more congenital anomalies in comparison with the babies from normal-conception (3-7). Hunt et al Showed that PAPP-A levels in those who have been cured by assisted fertility methods, such as IVF, were higher than those who become pregnant spontaneously. It could be a result of the intracytoplasmic sperm injection (ICSI) technique through microinjection that makes bleeding in zona pellucida thereby the placenta and biochemical tests in the first trimester can be affected (8). Human intervention and laboratory conditions in assisted reproductive techniques may have an impact on the fetus growth and development. (2).

Due to the importance of early diagnosis of congenital malformations, the lack of study in our country about embryo screening tests in the first and second trimesters among infertile women. This research conducted.

Therefore, the purpose of the study was to compare the results of embryonic health screening tests in pregnant women by using assisted reproductive techniques and natural pregnant women in Bandar Abbas city.

Methods

This was a case-control study was carried out doring April to November 2017. The study population included pregnant women referred to Ome Leila fertility and infertility center in Bandar Abbas city.

Two hundred pregnant women with assisted reproductive techniques as case group and 200 natural pregnant women as a control group were selected by a simple random sampling method. The inclusion criteria comprised: Iranian women with the Persian language, single pregnancy, having no specific disease related to pregnancy, and at the 21st-42nd week, performed both screening tests (the first-trimester screening and quadruple test in the second). Enough information about the goals of the study was provided and then written consent was taken.

A researcher-made checklist was used to record the data which contain personal and demographic information (such as mother and father's occupation and age, maternal body mass index, father's smoking, the length marriage, infertility history, duration of infertility, cause and type of infertility, serum levels of embryo screening tests, family history of marriage, and a mother's medical history). This information is obtained by interviewing with mothers, considering tests and sonographies, and health records. To have the probability of embryonic chromosonal abmormalities such as down syadrom, synrom, trisomy 18 and 13, in the first trimester, two markers (PAPP-A and free β-hCG) beside NT marker in ultrasonography were simultaneously measured. Then in the second trimester, four biochemical markers were measured (alpha-fetoprotein, free β-hCG, non-conjugated estradiol, and inhibin A).

To calculate the risk of disease, MOM (Multiple of the Median) software was used as an assessing indicator of the ratio of measured marker to the expected marker in a specific pregnancy week. Then, the data were encoded and analyzed by SPSS version 21. Statistical tests such as ANOVA, *t* test, and chi-square, were used. The significance level in all stages was ($P<0.05$).

Results

In the present study, the mean age of women was 31.3 ± 6.26 years and the men were 35.6 ± 6 years (Table 1).

The majority of women were housewives who had primary infertility and no history of smoking or underlying disease. In most of them, the body mass index was normal.

The results showed that there was no significant difference in the final findings between two groups in the first trimester. However, in the second one, it was higher in the case group ($P<0.001$) (Table 2).

The mean of all types of tests in the first trimester did not have any significant difference ($P>0.05$). However, in the second trimester, the mean of screening tests including β-hCG ($P=0.006$) and AFP ($P=0.018$) was higher in the case group than the control group. But there was no significant difference in the mean of Estradiol, Inhibin, NB and NT tests in the both groups (Table 3).

Discussion

Based on the cause of infertility, it is possible to get pregnant for infertile couples by using assisted reproduction technology. It is shown in various studies that children who are born through infertility treatments,

Table 1. Demographic Data in Both Case and Control Groups

Variable	Case Mean (SD)	Control Mean (SD)
Age of the woman (y)	31.3±6.26	28±6.0
Age of the man (y)	35.6 ± 6	32 ± 6.1
The length of marriage (y)	5.17 ± 8.86	5.0 ± 4.9
The length of infertility (y)	7.3±5.15	3.06±1.17

especially IVF, have reported more congenital anomalies than normal births. (7-12). Prevention of chromosomal abnormalities is only possible through doing the screening tests, detecting malformations, and terming this pregnancy with family consent. The purpose of the study was to determine the effect of assisted reproduction technology on screening tests in two groups of pregnant women. One who became pregnant by assisted reproductive methods and the other one included natural pregnant woman. The present study did not illustrate any significant difference in the use of these techniques on the screening tests in the first trimester. The study by Jose et al. (2005) also found that assisted reproductive methods did not affect the first-trimester biochemical tests (13). Also, a study by Ghisoni et al. (2003-2000) showed that the first-trimester biochemical tests, such as free B-hCG, PAPP-A levels, and NT were not significantly different among natural pregnant women or become pregnant by using assisted reproductive techniques (14). Our study showed that in the second trimester, there was a significant difference between the case and control groups. The probability of congenital anomalies was higher in the case group. The results showed that the mean between groups in the first trimester did not have any significant difference. However, in the second trimester, the mean of tests including β-hCG and AFP had a significant difference among them. It was higher in the case group than the control. The results of Räty et al which were similar to this study showed that by using IVF and ICSI, IVF in special, β-hCG was higher than in the control group. The level of AFP had approximately the same level. The number and time of embryo transmission may be effective on the marker level (15). One of the hypotheses is that in assisted reproductive techniques the dosage of gonadotrophin makes changes in the level of markers (16). The high levels of β-hCG and AFP markers could indicate the possibility of Down syndrome in fetuses resulted from assisted reproductive technology. This study showed that the use of assisted reproductive techniques did not have an impact on the mean of Estradiol and INHIBNE, NB, and NT.

Conclusion

The results of our study showed that embryonic health screening tests, especially β-hCG and AFP markers, will be affected by the use of assisted reproductive techniques. For couples who have a history of infertility and using these techniques, screening tests are essential in the first and second trimesters.

Authors' Contribution

SHS considered data gathering approaches and prepared the research proposal under management AK. ZKH writes the first

Table 2. Results of Embryo Screening Tests in the First and Second Trimester in Both Case and Control Groups

	Variable	Case No. (%)	Control No. (%)	Total No. (%)	*P* Value
First trimester	Test result				0.372
	Positive	10(2.5)	11(2.8)	21(5.3)	
	Negative	152(38)	221(55.3)	373(93.3)	
	Intermedia	4(1)	2(0.5)	6(1.5)	
Second trimester	Test result				0.001
	Positive	21 (5.3)	5 (1.3)	26 (6.5)	
	Negative	136 (34)	221 (55.3)	357 (89.3)	
	Others (intermediate and non-performing)	9 (2.3)	8 (2)	17(4.3)	

Table 3. Types of Embryo Screening Tests in the First and Second Trimester in Both Case and Control Groups

Variable		Case Mean (SD)	Control Mean (SD)	*P* Value
1st trimester	PAPPA	2609.47±5434.57	3265.78±4433.67	0.201
	β-hCG	786.80±4193.05	812.23±3449.84	0.947
	NT	1.16±0.34	1.22±0.63	0.252
	NB			
	Yes	164(41)	234(58.5)	0.172
	No	2(0.5)	0(0)	
2nd trimester	**ESTRADIOL**	4.44±16.65	3.01±2.44	0.203
	β-hCG	32090.62±43828.96	21903.65±15117.89	0.006
	Inhibin	269.46±279.49	21903.65±15117.65	0.153
	AFP	51.99±65.66	239.35±124.28	0.018

draft of the manuscript. SHS contributed the manuscript, and AK, ZA, and NR revised it. SHS edited the final manuscript. All of the authors contributed to the revised and confirmed the final version of the manuscript.

Conflict of Interests
No competing interests.

Ethical Approval
The ethical approval code was IR.PNU.REC.1398.079.

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Informed Consent
Enough information about the goals of the study was provided and then written consent was taken.

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