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Review article

Factors Contributing to the Failure of In Vitro Fertilization (IVF): A Review of Male, Female, and Laboratory-Related Causes  
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Abstract

Infertility is big problem with some couples, infertility is an inability to get pregnancy and live birth after one year of marriage. There are many causes for this problem. In vitro fertilization (IVF) is one of the process to treat infertility. In vitro fertilization is includes induction of the ovaries to produce numerous oocytes, than fertilize the oocytes and development of the embryo, finally transfer the embryo. The most important reasons for repeated failure in vitro fertilization (IVF) cycle are related to the male characteristics, such as low semen concentration low sperm motility and morphology of sperm, there is a relationship between sperm quality and IVF outcome. Most of the maternal factors that contribution in decrease implantation and IVF cycle are uterine anomalies, adhesions, septa, and many more. Other factors such as body mass index (BMI), and smoking status for failure IVF. In this study review some of the causes of failure In vitro fertilization.

Introduction

Around the world, many couples are suffer from problem known as infertility, approximately sixty to eighty million couples (1). Infertility is an inability to get pregnancy and live birth after one year of marriage (2)

In vitro fertilization (IVF) is the process that includes more than step, first step is induction of the ovaries to produce numerous oocytes, second step is fertilize the oocytes and development of the embryos in the laboratory, finally transfer the embryo into uterus (3). Before beginning in vitro fertilization cycle should be recorded a number of clinical factors such as patient age, body mass index (BMI), and smoking status, and also number of pregnancy, IUI (intrauterine insemination) attempts, spontaneous abortion, and live birth (4).

The most important reasons for repeated failure in vitro fertilization (IVF) cycle are related to the male characteristics, such as low semen concentration low sperm motility and morphology of sperm (5).

### Laboratory factors

In the laboratory there is a wide range of failure potential. Failure in fertilization (3), the sperm can't fertilize the oocytes for many reasons, including low sperm concentration, low sperm motility, and abnormal morphology of sperm(5,6). Also the failure after fertilization, including penetration the sperm of the oocyte membrane failure to fusion with ooplasm, or failure in fuse the nuclei of the sperm and oocyte. Also failure occur in cleavage of the embryo. Failure associate to embryos transfers (3).

### Embryos transfers

Embryos transfers at cleavage stage ( day 3), embryos as a "good" graded should be  $\geq 7$  cells with perfect symmetry cells and fragmentation (  $\leq 10$  %), or  $\geq 7$  cells with moderate symmetry cells and fragmentation ( 0 % ). Embryos as a "poor" graded are five or less than five cells with severely uneven symmetry cells and fragmentation ( more than 25 % ), or  $\leq 5$  cells with moderate symmetry and fragmentation ( 11-25 %).

Embryos transfers at blastocysts stage ( day 5 ), embryos as a "good" graded should be outer cells mass ( trophoblast ) consisted a few cells forming a loose epithelium or many cells forming a cohesive epithelium, and inner cells mass ( embryoblast ) comprised of many, tightly packed cells (7). Finally, embryos are as a "poor" graded when blastocysts had a very few cells in trophoblast or embryoblast, early blastocysts, and morula stage (8). This means embryos transfers in incorrect time or "poor" graded lead to failure implantation and therefore failure IVF cycle.

### Zona pellucida

Zona pellucida (ZP) is a glycoproteins that secreted from oocyte and granulosa cells on the surface of the oocyte. Zona pellucida hardens after fertilization to prevent polyspermy and protect the embryo until its implantation(9). The blastocyst hatches the zona pellucida when entered the uterine, for implantation in the endometrium. Increased zona pellucida hardness and thickness was cause to implantation failure and as a result to lower pregnancy rates (10). Thus, one of the possible cause for implantation failure after IVF cycle is the failure of the zona pellucida rupture (11). There are different techniques were used to weaken the zona pellucida or create an opening in zona pellucida in order to assist hatching (AH). Er:Yag laser system used for assist hatching lead to increase in implantation rates and pregnancy rates (12). Increase the implantation and pregnancy rates by assist hatching that performed in different techniques (mechanical and chemical) (13,14).

### Male factors

Male factors infertility such as oxidative stress, abnormal sperm chromatin structure, DNA damage, and altered gene expression can effect on implantation and pregnancy rate. Deformities in the testes, vas deferens, and epididymis are sure contribute in decrease fertilization rate and implantation because its lead to abnormalities in sperm, then failure IVF cycle (15).

Many studies have shown there is a relationship between sperm quality ( sperm concentration, morphology, and motility) and IVF outcome(6).

Measure of the amount of damaged DNA in sperm is DFI ( the DNA fragmentation index of sperm ). An increase in the miscarriage and a decrease in the implantation and pregnancy rate are associated with DFI (16).

Pregnancy loss and problems in embryo development could be caused by abnormalities in paternal epigenome that linked with male factor infertility(17).

Also abnormalities in seminal plasma cytokines can affect the pregnancy rate (18,19).

### Female factors

Most of the maternal factors that contribution in decrease implantation and IVF cycle are uterine anomalies, adhesions, septa, and many more. The contribution of the uterine anatomical anomalies to failure of implantation is variable. Surgical correction of such findings ( an example adhesion, protruding submucous fibroids) was beneficial (20). The pregnancy rate were higher than initially before surgery (21).

### Hydrosalpinges

Hydrosalpinges is a condition where fluid accrues in both or one ovarian tubes (fallopian tubes), forming a blockage. **The wife with hydrosalpinges have lower implantation and pregnancy rates perhaps due to** the harmful effect of the hydrosalpinges fluid has on both endometrium and embryo (22,23).

The tubal surgery to women with hydrosalpinges increased pregnancy rate and live birth rate before IVF compared with women no treatment (24). Some organization was recommend to surgically remove fluid-filled distally occluded tubes before any IVF treatment (25).

### Obesity

**Obesity is defined as a body mass index (BMI) equal to or greater than 30, according to the world health organization (WHO)** (26). Based on many studies that conducted on obese women, it was found that obesity is one of the most important causes of IVF failure.

Study was conducted on a numbers of obese women (BMI $\geq$ 30). It is demonstrated that there is adversely affected by the obesity on the implantation and pregnancy rates, as well as on live birth rates (27). Other studies confirmed these results with a decrease in rate of implantation and pregnancy in obese women (28,29). One of the largest studies conducted on obesity and its effect on pregnancy rates after IVF cycles. Including men, as it continued for several years. The effect of obese women on the pregnancy rates after IVF cycles has been clearly proven, while obese men have no effect (30).

### Cigarette smoke

The women who want to get pregnancy should stop smoking and also stay away from exposure to secondhand tobacco smoke (31). The smoking effect on the himself smoker as well as the women that suffer from secondhand tobacco smoke exposure who trying to become pregnancy (31).

There are relationship between implantation failure, and smoking and secondhand tobacco smoke exposure. Implantation failure increase with women exposure to secondhand smoke, compared with women that unexposed. Also, decrease in a live birth with women those exposure (32).

High probability of spontaneous miscarriage and low probability of live birth in women who smoke, this data is very important to prevent some of the causes of IVF failure (33).