# Prevalence of antiphospholipid antibodies in failed IVF/ICSI and associating Sonohysterographic picture

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# INTRODUCTION

Infertility is a common problem affecting approximately 13-14% in couple's reproductive age. The classic definition of infertility is the inability to conceive after 1 year of unprotected intercourse. (**Abma et al., 1997**).

Studies of populations of patients with infertility indicates that approximately 10-25% have unexplained infertility, 20-30% ovulatory dysfunction, 20-25% tubal damage, 10-50% sperm dysfunction, 5-10% endometriosis, 5% cervical mucous problems and 5% coital dysfunction while a large number of human pregnancies fail during implantation stage because the uterine endometrium is unreceptive to the implanting embryo **(Jacobs and Balen 2003)**.

The past 50 years have been a revolution in the regulation of the female reproductive system with the development of steroid and now gonadotrophin therapies. These advances have led to hormonal contraception, hormone replacement therapy, ovulation induction and have facilitated the growth of assisted reproduction **(Smith and Brien 1998).**

Recent development in infertility treatment have further diminished the consequences of sever male factor infertility.

In-Vitro Fertilization (IVF) presented a new hope to many couples who would otherwise have absent or minimal chance of conception.
It is a fertility procedure which first succeeded as recently as 1978 by Dr. Edward (an embryologist) and Dr. Steptoe (a gynecologist) in England embryologist. (**Steptoe and Edwards 1979**).

IVF/embryo transfer (IVF/ET) treatment involves development of multiple follicles, oocyte retrieval and ET after fertilization. Since then the technology has been further refined and developed by physician and embryologist.

Intracytoplasmic sperm injection (ICSI) is one of the modalities of assisted reproductive technique which aims to the treatment of couples in whom the male partners has azoospermia or sever oligospermi. ICSI is also indicated for men with significant antisperm antibodies, low sperm motility, or significantly abnormal sperm morphology. ICSI is used when poor fertilization occurs with regular insemination techniques in the laboratory. Sperm can be obtained from the ejaculate or directly from the epididymis. Recently, success was obtained with spermatids from testicular biopsies. (**Palermo et al., 1992**)

Failure of conception despite the repeated transfer of apparently good quality embryo is a significant clinical problem in vitro fertilization (IVF) practice. Clinically, the definition of recurrent treatment failure varies but usually includes a number of completed IVF-embryo transfer (ET) cycles and/or the cumulative number of embryos transferred during the unsuccessful treatment. (**Stern et al., 2003**) (**Raziel et al., 2002**).

Success rate in IVF remain stubbornly low, providing distress both for the individual concerned and for the economics of the women ´s health.

There is considerable interest in the potential causes of recurrent implantation failure and in strategies that may improve implantation through changes in clinical and embryology practice. (**Scott 2002**)

IVF success is dependent on the coordinated development of embryo and endometrium and persistent abnormalities of either may lead to recurrent treatment failure. (**Ng et al., 2006**).

Because of the major medical, emotional and financial implication of IVF treatment, numerous studies addressed different methods of trying to predict the outcome of IVF cycles, and to define possible risk factors that may underlie any poor outcome, in a hope to improve the success rates of IVF. Some of these include immunological testing and treatment. **(Urman 2005 a).**

Increased levels of autoantibody were initially described in patients with infertility due to endometriosis, but recurrent spontaneous abortion (RSA) and infertility patients overall have higher levels of autoantibody than do fertile woman **(Gleicher et al., 1989)**.

Autoantibody included in infertility screening often include ANA, APL, antithyroid antibodies, antisperm antibodies, and antizonal antibodies **(Kutteh 2002)**.

An increased prevalence of APL in patients with infertility has been shown in a large number of studies. Prevalence of APL in normal, including healthy pregnant women, is about 2% to 5%; in patients with RSA, prevalence is 15% to 20% (**Branch and Khamashta 2003)**.

The specific APL measured in these studies range from the generally accepted ACL and LA to large panels of multiple autoantibodies directed against various phospholipids. Some authors, however, feel that certain APLs distinct from ACL and LA are more predictive of IVF failure **(Balash and Cervera 2002)**.

Studies including only IVF failure patients show roughly the same range of prevalence rates as general infertility patients, from 10% to 32%. However, direct comparison studies do suggest a higher prevalence in patients with implantation failure **(Chilcott et al., 2000)**.

**Di Simone and coworkers** demonstrated in vitro binding of APS to human trophoblast in a dose-dependent manner, adversely affecting trophoblast invasiveness and cytotrophoblast differentiation into syncytium (**Di Simone et al., 1999)**. The same group has further demonstrated changes in transcription and translation of cell adhesion molecules, with resulting altered expression leading to failure of blastocyst implantation **(Di Simone et al., 2002)**.

Although early clinical studies and experimental work support a role for APL pathogenicity in IVF implantation failure, recent studies do not show either a difference in IVF cycle outcome based on APL status, or a benefit to treatment of APL positive patients with heparin and aspirin during IVF **(Munther 2006)**.

To optimize the outcome of an IVF cycle it is desired that the uterine cavity contain no lesions and have receptive endometrium. Structural uterine anomalies seen in 1.3% of patients undergoing IVF–frozen embryo transfer (FET) have been reported to be associated with implantation failure and early pregnancy loss, as well as obstetric problems **(Valenzano et al., 2006)**.

Assessment of tubal patency and evaluation of the uterine cavity should be part of all infertility investigations, particularly when transferred embryos are of good quality; recurrent implantation failure may be attributed to pathological lesions of the uterine cavity as fibroids **(Urman 2005a).**

Difficult embryo transfer secondary to cervical or uterine pathology adversely affect the outcome in women undergoing IVF–embryo transfer **(Spandorfer et al., 2003).**

Uterine abnormalities can be detected by hysteroscopy, it has therefore been suggested that all women should undergo diagnostic hysteroscopy before IVF treatment. (**Golan et al., 1992**).

Sonohysterography referred to as saline-enhanced ultrasonography, is being used with increasing frequency for investigation of infertility and other gynecological indications, it allows good differentiation between congenital and acquired endometrial cavity pathology. (**Gaucherand et al., 1995).**

Sonohysterography is similar to hysterosalpingography (HSG) in its effectiveness for evaluating tubal patency and superior to HSG for assessing intrauterine abnormalities.

Also advantages of SHSG over HSG include the ability to assess extra-uterine structures, lack of ionizing radiation, better tolerability by the woman being examined and can offer detailed assessment of the female pelvis, so has the potential to replace HSG as a routine, first-line infertility investigation. (**Case and Pierson 2003**)

Uterine cavity evaluation using saline is the method of choice; it is simple, safe and cheap outpatient method prior to any following invasive procedure or even hysterosalpingography. **(Radic et al., 2005)**

In experienced hands, SHG is an easy, safe, and well-tolerated alternative to diagnostic hysteroscopy in the initial evaluation of uterine cavity in infertile patients. (**Ragni et al., 2005**).