

ORIGINAL PAPER

Sexual intercourse before embryo transfer in assisted reproductive technology might enhance probability of pregnancy: An observational study

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Summary

Background: Modifying the maternal immune system is necessary to facilitate embryo implantation. Modifying the immune system can occur in several ways, including maternal exposure to the partner's seminal plasma. Seminal plasma exposure can occur through sexual intercourse. To prove this theory, we investigate the effect of sexual intercourse on the chances of successful in vitro fertilization (IVF) in both fresh and frozen embryo transfer (ET) groups in terms of biochemical and clinical pregnancy.

Methods: This is an observational analytical study with a retrospective cohort study design. This study compared biochemical and clinical pregnancy in patient groups who had sexual intercourse with those who did not have sexual intercourse during the IVF process. This study involved 132 participants.

Results: The results of this study reported that there was no significant difference in pregnancy rates between patients who had sex before ET and those who did not have sex before ET.

However, patients who experience orgasm during sex show significant rates of biochemical ($p = 0.009$) and clinical pregnancy ($p = 0.027$) rates.

Conclusions: Sexual intercourse did not show a significant difference between the groups who had sex before ET and those who did not have sex, but the experience of orgasm every time they had sex recently had a positive impact on reproductive health, especially pregnancy.

KEY WORDS: In-vitro fertilization; Sexual intercourse; Embryo transfer; Reproductive health; Orgasm.

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BACKGROUND

One of the most commonly used methods to help infertile couples is *in vitro* fertilization (IVF). IVF is reported to succeed in only 30-40% of cases (1). Several factors influence the success rate of IVF. According to Crawford et al, one of the most critical processes for the success of IVF is embryo implantation; even if the quality of the embryo is excellent, implantation will fail if the endometrial receptivity is insufficient (2).

Research reports that endometrial receptivity is closely

linked to the maternal immune response. The embryo that will implant in the endometrial wall is likened to an allograft in the maternal body. This requires a balance of immune responses in the process so as to avoid any form of attack on the embryo (3). The immune response that plays a dominant role in this process is T-reg; the number of dominant T-reg will produce *interleukin-10* (IL-10) and *tumor growth factor-beta* (TGF- β) and suppress Th-1 so that the levels of *interferon-gamma* (IFN- γ), *interleukin-12* (IL-12), *interleukin* (IL-2), and *tumor necrosis factor-beta* (TNF- α) would become low (3, 4). T-cell regulation and the involved cytokines contribute to the implantation process. T-reg cells also suppress the proliferation and function of leukocyte subsets such as CD4 T cells, CD8 T cells, B cells, and *natural killer* (NK) cells. T-reg cells influence the function of *dendritic cells* (DCs) and macrophages (4, 5). If this does not occur, implantation will become difficult or, in some cases, hemorrhage will occur, leading to embryonic failure (4, 6, 7). Experts argue that modifying the maternal immune system is necessary to facilitate embryo implantation. Modifying the immune system can occur in several ways, including maternal exposure to the partner's seminal plasma. Exposure to seminal plasma, such as during intercourse, has been reported to improve embryo implantation (8, 9). This is because seminal plasma contains many biomolecules, such as TGF- β , that influence the immune system in the endometrium. Several studies have investigated the relationship between seminal plasma exposure and pregnancy success rates. However, because they used different methods, the *embryo transfer* (ET) time group (fresh or frozen) was also not uniform, leading to different results (2, 10). In light of the above, we conducted a study to investigate the effect of sexual intercourse on the chances of successful IVF in both fresh and frozen ET groups in terms of biochemical and clinical pregnancy in Indonesia.

MATERIALS AND METHODS

Design of the study

This is an observational analytical study with a retrospective

cohort study design. This study compared biochemical and clinical pregnancy in patient groups who had sexual intercourse with those who did not have sexual intercourse during the IVF process. The study was conducted at *Ferina Mother and Child Hospital, Surabaya*, from September to November 2022. The study was approved by the ethic committee with approval number: 193/EC/KEPK/FKUA/2022.

Sample size and criteria

This study's participants were RSIA Ferina patients who participated in the assisted reproductive technology program as couples who followed the procedure of both fresh ET and frozen ET with blastocyst embryos. We excluded patients with the following criteria: 1) high D-dimer, 2) experienced pain (cough, runny nose, fever) during and after the procedure (observation period), 3) non-compliant according to the ovarian stimulation procedure, 4) husband with obstructive azoospermia, and 5) husband with leukospermia semen analysis examination results. Participants were included consecutively according to the research selection criteria until the required number of participants was met. This study used a test for a difference between two population proportions (11), therefore, by using reference values from previous studies (12), the minimum number of participants in each group was estimated in 45.

Procedure

Patients had initially undergone menstrual examination and stimulation until it was declared that the follicles were developing and prepared for ovum pick-up. The collected oocytes were then fertilized to obtain embryo(s). The researcher explained the patients who fit the inclusion and exclusion criteria regarding the research procedure. Before the patient underwent the embryo transfer procedure, the patients were told they can have sexual intercourse 1-5 days before the ET procedure. However, it was the patients' choice to have sexual intercourse or not. The determination of 1-5 days interval before ET was based on previous studies that conducted exposure to seminal plasma after *ovum pick-up* (OPU), where the distance from OPU to ET procedures was 3-5 days in fresh embryo transfer procedures (13, 14).

After receiving ET, the patients were placed in the one-day care unit. The researcher then conducted an interview on the patient regarding the patient's sexual history during 1-5 days before ET, including the frequency and whether she had an orgasm or not. We only interviewed the patients who received blastocyst embryo. After that, the patients were observed until 11-14 days after ET, and then the beta-hCG test was carried out using the VIDAS[®] HCG kit using the ELFA (*Enzyme Linked Fluorescent Assay*) principle. Thus, the patient would be declared pregnant if the beta-hCG level is 25 mIU/mL. Then 5-6 weeks later, ultrasound monitoring was conducted on patients who had biochemical pregnancy to detect the gestational sac. The patient was declared clinically pregnant if gestational sac was positive.

Data analysis

The first analysis was univariate; it was conducted to assess the demographic data and the characteristics of the study participants. The second analysis was a bivariate

analysis to analyze the association of sexual intercourse and other sexual intercourse parameters with biochemical (beta-hCG) and clinical (gestational sac) pregnancy; the test used was chi-square or Fisher's exact test.

RESULTS

The couples interviewed in this study were primary or secondary infertile couples who were undergoing IVF at Ferina Mother and Child Hospital. The participants were 132 couples. The participants were divided into two groups. The first group included 45 couples who had sexual intercourse 1-5 days prior ET, while the second group included the remaining 87 couples who did not have sexual intercourse. The characteristics of the participants can be seen in Table 1.

Based on Table 2, 9.85% of the participants had sexual intercourse and were declared pregnant, 24.24% had sexual intercourse and were not declared pregnant, 23.48% did not have sexual intercourse and were declared pregnant, and 42.42% did not have sexual intercourse and were not declared pregnant. The results of the chi-square test showed $p = 0.436$, with $RR = 0.81$ (95% CI 0.46-1.35), which means that there is no significant relationship between intercourse before ET and the success rate of biochemical pregnancy.

Table 1.
Characteristics of the participants.

Variable	Having Sex (n = 45)	Not having sex (n = 87)
Age of Wife (years)	33.78 ± 3.57	34.23 ± 5.0
Age of Husband (years)	36.20 ± 3.77	38.17 ± 6.34
BMI of Wife (kg/m ²)	26.08 ± 3.63	25.43 ± 3.85
Type of Infertility		
Primary	25 (55.5%)	20 (44.5%)
Secondary	53 (60.9%)	34 (39.1%)
Duration of Infertility (years)	6.16 ± 3.43	6.05 ± 3.43
Infertility Factor		
Wife	18 (40%)	36 (41.37%)
Husband	8 (17.8%)	12 (13.8%)
Mix	18 (40%)	32 (36.78%)
Unexplained	1 (2.2%)	7 (8.05%)
Type of Embryo Transfer		
Frozen	38 (84.45%)	46 (52.87%)
Fresh	7 (15.55%)	41 (47.13%)

Table 2.
Analysis of pregnancy in relation to sexual intercourse before ET.

Variable		Beta hCG > 10		p-value	GS		p-value
		Positive	Negative		Positive	Negative	
Sexual	Yes	13	32	0.436	9	36	0.590
	No	31	56		66		
Fresh ET	Yes	4	3	0.439	6	32	0.656
	No	17	24		7	39	
Frozen ET	Yes	9	29	0.489	6	32	0.942
	No	14	32		7	39	

GS: Gestational sac.
*p-significance < 0.05 using chi-square test.

In the group who had sexual intercourse 6.82% were declared clinically pregnant and 27.27% were not declared pregnant. In the group that did not have sexual intercourse 15.91% were declared pregnant and 50% were not declared pregnant. The chi-square test obtained a value of $p = 0.59$, with $RR = 0.83$ (CI 95% 0.41-1.60). These results indicate that there is no significant relationship between these two variables.

In the group who regularly had sexual intercourse (2-3x/week) and 15.91% were declared pregnant, whereas those who were not declared pregnant were 34.09%. In the group who rarely had sexual intercourse (0-1x/week) 17.42% were declared pregnant whereas those who were not declared pregnant were 32.58%. The chi-square test results obtained a value of $p = 0.59$, with $RR = 0.91$ (CI 95% 0.56-1.48). In the group that regularly had sexual intercourse 12.88% were declared clinically pregnant, and those who were not declared pregnant were 37.12%. In comparison, in the group that rarely had sexual intercourse 9.85% was declared pregnant and those who were not declared pregnant were 40.15%. The chi-square test results obtained a value of $p = 0.406$, with $RR = 1.30$ (CI 95% 0.70-2.46) (Table 2).

In addition, in the group who stated that they always orgasmed every time they had sexual intercourse 22.73% were declared biochemically pregnant and 29.55% were not declared pregnant were 29.55%. In comparison, in the group who did not orgasm every time they had sexual intercourse or orgasmed only sometimes, 10.61% were declared biochemically pregnant and 37.12% were not declared biochemically pregnant. The chi-square test results obtained a value of $p = 0.009$, with $RR = 1.96$ (CI 95% 1.17-3.37). Regarding clinical pregnancy, in the group who stated that they always orgasmed every time they had sexual intercourse 15.91% were declared clinically pregnant and 36.36% were not declared pregnant. In the group who did not orgasm every time they had sexual intercourse or orgasmed only sometimes, 6.82% were declared clinically pregnant and 40.91% were not declared pregnant. The chi-square test results obtained a value of $p = 0.027$, with $RR = 2.13$ (CI 95% 1.09-4.29) (Table 3). We assumed that there is a correlation between orgasm and the probability of pregnancy. However, we agree that it could not be explicitly concluded that orgasm is a positive factor for enhancing pregnancy. We can only simply argue that orgasm is a condition that indicates that both psychological and social conditions are favourable.

Table 3.
Analysis of orgasmic phase in intercourse before ET with pregnancy.

Variable	Beta hCG > 10		p-value	GS		p-value	
	Positive	Negative		Positive	Negative		
Intensity of sexual intercourse	Routine	21	45	0.711	17	49	0.406
	Infrequent	23	43		13	53	
Orgasmic	Yes	30	39	0.009*	21	48	0.027*
	No	14	49		9	54	

GS: Gestational sac.
*p-significance < 0.05 using chi-square test.

DISCUSSION

Our study aimed to compare the effect of sexual intercourse as seminal plasma exposure to the female reproductive system on the success rate of pregnancy, both biochemical and clinical, in women undergoing assisted reproductive technology (ART) programs. This recent study divided the participants into two groups. The first group was the group who had sexual intercourse 1-5 days before the ET procedure, and the second group was the group who did not have sexual intercourse 1-5 days before ET.

In addition, our study also analyzed the frequency/habit of sexual intercourse outside the ART program, the quality of sexual intercourse in the form of achieving orgasm, the type of infertility, and the ET method (fresh or frozen) on pregnancy success (biochemical and clinical).

Our study reported 45 (34.09%) patients had sexual intercourse before ET. Some of the reasons patients did not have sex before ET were the fear and anxiety about sexual intercourse that it might be causing IVF program failure. The similar phenomenon was also reported by *Courbiere et al.*, which states that 47% of the patients had difficulty having sex during the IVF program, and 44% experienced a decreasing desire to have sex with their partner (15). *Marci et al.* also reported the same finding, stating that couples had experienced sexual disorders even at the beginning of infertility treatment (16).

Another finding in our study is that there was no association between sexual intercourse before ET and both biochemical and clinical pregnancy rate. We reported $RR = 0.81$ (95% CI 0.46-1.35) in biochemical pregnancy and $RR = 0.83$ (95% CI 0.41-1.60) in clinical pregnancy. Similar results were also reported in a study by *von Wolff et al.* (2013) who reported $RR = 0.92$ (CI 95% 0.63-1.34) in clinical pregnancy (17).

However, a study in China by *Sun et al.* reported different results. Sun et al found that sexual intercourse significantly affected pregnancy success in the ART program ($p = 0.005$ in biochemical pregnancy and $p = 0.045$ in clinical pregnancy) (18).

So far, the theory that explains how sexual intercourse can affect the chance of pregnancy is the induction of the immune system of the reproductive organs (uterus) in the process of pregnancy (19). Seminal plasma contains immune substances such as TGF- β which is indispensable in the implantation process, as well as other molecules such as PGE2 and DC (4). In addition, sexual intercourse also increases uterine activity such as contractions that have an impact on embryo implantation (20).

However, the different results in our study might be due to the variation of the length of the interval between sexual intercourse and ET, which is not homogeneous. Our study established an interval between sexual intercourse and ET of 1-5 days. Most participants in this study had sexual intercourse more than 24 hours before ET. In fact, some studies supporting a significant role of sexual intercourse, reported the most effective interval between sexual intercourse and ET to be 12-24 hours. As reported by *Sun et al*, *Aflatoonian et al* and *Tremellen et al*, there were very few patients who consciously had sex 12-24 hours before ET because many patients were worried that sex within this period would cause failure of ET (18, 21, 22). Another possible reason for the non-significant results is

the type of ET performed in our patients. The results of the study by Sun et al were significant in the group of patients who performed frozen embryo transfer procedures, while in our participants, both frozen and fresh embryo transfer groups were analyzed simultaneously (18).

Furthermore, the study by Sun et al. compared couples who had sex and used contraception with couples who did not have sex before ET. So, this study was biased regarding whether pregnancy success was due to seminal plasma exposure or other factors.

Our study attempted to adjust the effect of the variable of sexual intercourse evaluating both biochemical and clinical pregnancy, although the small sample size could not have maximized this adjustment (18).

In addition, another possible cause of bias is the difficulty to control the factors beforehand, such as the stimulation protocol used in patients, especially in the fresh ET group. Some studies, such as Lan et al., Ou et al., and Youseff et al., reported that long protocol significantly increased IVF success compared to short protocol (23-25).

Psychological aspects may also contribute to the successful outcomes of IVF programs. Matthiesen et al. reported that there is a significant relationship between stress and the chances of IVF success (26). The same finding was also reported by Saleem et al. in the Tunisian population following an IVF program. Stress and anxiety were negatively correlated with success rates (27). At the same time, Courbiere et al. stated that patients who follow IVF programs are vulnerable to psychosocial burdens that can affect their daily life (15).

Another contributing factor that may affect IVF success is BMI. Bashiri, Halper, and Orvieto stated that uncontrolled BMI affects IVF success (28).

In our study, we did not evaluate length of protocol, psychological factors and BMI that could be factors causing the difference in results with other studies.

It has been hypothesized that embryo implantation is strongly influenced by endometrial receptivity. Endometrial receptivity depends on immune factors.

Also, the balance of immune factors in the endometrial wall itself is influenced by various factors (3). One of the components of immune system, called T-reg cells, is known to be a key factor to successful implantation.

T-reg cells play a role in regulating equilibrium in the major histocompatibility complex (MHC) mechanism (3). Exposure to seminal plasma allows the activation of T-reg cells in the female reproductive organs (uterus), thus supporting embryo implantation. Another theory states that sexual intercourse is associated with cervicovaginal immune mediators in young female populations (29). Frequent sexual intercourse also causes a decrease in IgA at ovulation compared to infrequent or no intercourse. It also affects the expression of Th-2-like cytokine ratios (IFN- γ < IL-4), P-E2 ratios in the luteal phase compared to other phases (30).

Based on this hypothesis, regular or continuous exposure to a partner's seminal plasma might alter the regulation of T-reg cells in the female reproductive organs. Thus, the frequency of sexual intercourse might affect the immune status/condition in the uterus. There are still very few studies that report about these findings, especially in the ART population group. The study of Konishi et al. report-

ed that there was a significant relationship between coitus frequency and increased chances of pregnancy. However, these results were tested in populations with natural cycles or without the ART program (31). However, the relationship between the two variables seems to be insignificant in this present study. This may be due to lack of information related to the frequency of sexual intercourse. The information explored in this study was the history of intercourse in the past before the study participant started ART measures.

The association of sexual activity up to orgasm with the success rate of the ART program has not been widely studied. Our study reported that orgasm had a significant association with biochemical and clinical pregnancy. Frequent/always orgasmic partner sexual activity is associated with a healthy and supportive quality of partner life (32), while a healthy and supportive quality of partner life is needed to maintain the mental state of the study patients in undergoing the ART program. Levin also states that semen deposition and uterine contractions during orgasm cause mood changes in women (33). In addition, some theories state that orgasm also facilitates the release of hormones, such as oxytocin, that affect emotions in women. Women with a history of orgasm are reported to be happier and avoid stress (34). The result of the study still need further investigation despite it is significant. Also, we argue that orgasm is simply a condition that indicates that psychological and social conditions are favorable.

The Fertility Society of Australia notes that the mental quality of couples undergoing ART affects pregnancy outcomes (35). This may be the reason why orgasm can affect ART outcomes. In addition, several hypotheses state that orgasm can also affect the human immune system. Orgasm increases the number of absolute leukocyte sources and natural killer cells in blood vessels. However, the levels and changes in the immune system of female reproductive organs have not been reported (36).

We still realized that there are limitations in our study which is an observational study designed with a retrospective cohort. The selection of participants to be included in the groups who were sexually active and non-sexually active groups before IVF was voluntary rather than randomized being a disadvantage when compared to similar studies. In addition, information about sexual intercourse is often considered private for patients living in Indonesia. Consequently, the information shared about sexual life could be biased because patients are not honest about the information provided. Beside this, information about their sexual life is still based on recall memory.

Finally, a result of the study that should be transferred to the patients is that they should not be afraid to have sexual intercourse before embryo transfer, as was previously reported (37), because even if sexual intercourse does not have an apparent positive effect on pregnancy, it is not proven to have a harmful effect and may even have a positive effect on the psychological and relationship welfare of the couple.

CONCLUSIONS

The results of our study did show no significant difference between having sex before ET in terms of chemical and

clinical pregnancy chances. However, reaching orgasm during intercourse in recent sexual life has a positive impact on the couple's life and could also favourably impact on pregnancy probabilities although the significance of this finding still needs further investigation. Exposure to seminal plasma through sexual intercourse is not utterly uncorrelated with pregnancy, therefore also this still needs further investigation. Nevertheless, from a positive point of view, couples do not need to be afraid of having sex before ET because it does not have a negative effect but provide a better quality of life for couples.

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