

**ORIGINAL RESEARCH:****Comparison of pregnancy rates on day 3 and day 5 embryo transfer in In Vitro Fertilization (IVF)****Audia Mumtaz Rifasky<sup>1</sup>, Puspa Wardhani<sup>2</sup>, Ashon Sa'adi<sup>3</sup>, Ninik Darsini<sup>4</sup>, Hamdani Lunardhi<sup>4</sup>, Zakiyatul Faizah\*<sup>4</sup>**

<sup>1</sup>Medical Program, Faculty of Medicine, Universitas Airlangga, Surabaya, Indonesia <sup>2</sup>Department of Clinical Pathology, Faculty of Medicine, Universitas Airlangga, Surabaya, Indonesia. <sup>3</sup>Department of Obstetrics and Gynecology, Faculty of Medicine, Universitas Airlangga Dr. Soetomo General Hospital, Surabaya, Surabaya, Indonesia. <sup>4</sup>Department of Medical Biology, Faculty of Medicine, Universitas Airlangga, Surabaya, Indonesia.

**ABSTRACT**

**Objectives:** To identify the success rates of pregnancy on the third and fifth day embryo transfer at Graha Amerta Hospital, Surabaya, Indonesia.

**Materials and Methods:** This study used comparative cross sectional design. Data were taken from medical record of IVF participants who met the inclusion and exclusion criteria at Graha Amerta Hospital for the period of January 2016 - December 2016.

**Results:** Successful pregnancy rates were found in this research. The embryo transfer on the third day and the fifth day were 35% and 49.3% respectively. In other words, the rates of pregnancy success were not affected by embryo transfer on the third day and the fifth day in the medical record sample as it had p value of 0.090.

**Conclusion:** Embryo transfer on the third and fifth days had the same rates of pregnancy success in IVF participants at Graha Amerta Hospital, Surabaya, Indonesia.

**Keywords:** IVF; day 3; day 5; embryo transfer

**ABSTRAK**

**Tujuan:** untuk mengetahui tingkat keberhasilan kehamilan pada embrio transfer hari ketiga dan kelima di RS Graha Amerta, Surabaya, Indonesia.

**Bahan dan Metode:** Penelitian ini menggunakan studi analisis komparasi n (comparative study) cross section. Data yang digunakan yaitu rekam medis peserta IVF yang memenuhi kriteria inklusi dan eksklusi di RS Graha Amerta periode Januari 2016 – Desember 2016.

**Hasil:** Tingkat kehamilan yang berhasil ditunjukkan dalam penelitian ini, yaitu transfer embrio pada hari ketiga dan hari kelima adalah 35% dan 49,3% masing-masing. Dengan kata lain tingkat keberhasilan kehamilan tidak terpengaruh oleh transfer embrio pada hari ketiga dan hari kelima dalam sampel rekam medis. Hal ini dapat dilihat dari nilai P yang bernilai 0,090. jika diambil 0,05.

**Simpulan:** Transfer embrio pada hari ketiga dan kelima memiliki tingkat keberhasilan kehamilan tidak bermakna pada peserta IVF di RS Graha Amerta, Surabaya, Indonesia.

**Kata kunci:** IVF; hari ke 3; hari ke 5; transfer embrio

**\*Correspondence:** Zakiyatul Faizah, Department of Medical Biology, Faculty of Medicine, Universitas Airlangga, Jalan Prof dr Moestopo 47, Surabaya 60131, Indonesia. E-mail: faizbiomed@yahoo.com

## INTRODUCTION

Currently, infertility rate in Indonesia is 10-20% of married couples, and from the 10% it turns out that 10%-20% need Assisted Reproductive Technology (ART), including the newly developed In-Vitro Fertilization (IVF), which is now widely used for infertility treatment.<sup>1</sup> Infertility is defined as a condition marked by attempts to have regular sexual relations by not using protector and establishing a clinical pregnancy for 12 months but ending in failure and also because an individual or the partner has disability to reproduce.<sup>2</sup> The simple understanding of IVF is the removal of the ovum out from the ovary and then integrating it with the sperm cells in the laboratory to become an embryo.<sup>1</sup> In its implementation, embryo transfer is the phase that is considered to determine the success, while the pre- or post transfer activities are also very influential in its success. In general, embryo transfer is carried out on 5th day when the embryo enters blastocyst stage.<sup>3</sup> Because the longer the IVF process, the more difficult to breed the embryo until day 5, the embryo transfer is carried out on day 3, although at that time the implant rate is relatively low.<sup>4</sup> One study suggest that pregnancy rates and high implantation can be achieved by embryo transfer on day 3 and day 5. The level of implantation on third and fifth day of transfer is the same.<sup>5</sup> These studies were conducted to observe IVF outcomes where high positive success rate of beta-hCG and embryo transfer played an important role for this success. Thus, the best most suitable embryos were planted on day 3 and day 5. The main aim of this study was to analyze the success rates of pregnancy on the third and fifth day embryo transfer at Graha Amerta Hospital, Surabaya, Indonesia.

## MATERIALS AND METHODS

This study used a comparative cross-sectional design, which used total sampling of IVF participants at Graha Amerta Hospital, Surabaya, in 2016. Data were collected using medical records, which had been subjected to inclusion and exclusion criteria. The data were entered in Microsoft Excel and analyzed statistically using SPSS 16. This study received ethical approval from the Health Research Ethics Commission of the Dr. Soetomo Hospital, Surabaya, with ethical clearance letter number: 0705/KEPK/X/2018.

## RESULTS AND DISCUSSION

From medical records of January 2016 - December 2016, 256 data were obtained but only 139 samples of IVF participants in Graha Amerta Hospital, Surabaya,

Indonesia, who had completed medical record data and matched the inclusion and exclusion criteria. The sample needed were those with details of beta-hCG transfer embryos on third day and beta-hCG embryo transfer on fifth day. Data on IVF participants are presented in Table 1 and Table 2, showing p value of  $>0.05$  that there are no significant difference between embryos transfer on third day and embryos transfer on fifth day with pregnancy success rates in medical record samples. This finding was in line with a study by Dahiya et al. who found that embryo transfer day did not affect initial beta-hCG value.<sup>6</sup> However, another previous study did show that the stage of embryo development was affected significantly by embryo transfer day 3 or embryo transfer day 5.<sup>7</sup>

The embryonic cell division stage, which divided into 8 cells, 10 cells, 12 cells, 16 cells, morula and blastosis when it met the time of embryo transfer in IVF process, also does not affect the success rate of pregnancy. The same response was also shared by other researchers that live births and pregnancy success rates for embryo transfer at the blastocyst phase were the same as embryo transfer during the cleavage phase.<sup>8</sup> However, there are also other studies that proved that the blastocyst phase could produce higher pregnancy success rates compared to other stages of embryonic cell division.<sup>9</sup> Other studies suggest that the quality of embryo seen on the third day is one of the most effective predictors for determining pregnancy success, but the combination of parameters would be better as a predictor of pregnancy success.<sup>10,11</sup> The same opinion shows that implantation in embryo transfer on the third day significantly illustrates better outcomes at clinical pregnancy rates and is a good benchmark for providing information and helps in distinguishing good embryonic morphology as candidates for embryos transfer.<sup>12</sup>

Because the third day can be expressed as a predictor, if the embryo produced is good and abundant on the third day, it can be waited for and developed until the blastocyst stage and then the embryo transfer can be carried out. However, if on the third day the embryos are produced less and of poor quality, it is better to transfer embryo at that stage since the condition of embryonal development in the endometrium is much better than outside. Therefore, the embryo can be planted before the blastocyst stage and still be successful because the embryo and endometrium are in a good condition. However, other studies have suggested that pregnancy outcomes after the fifth day embryo transfer resulted in a higher value than the third day embryo transfer.<sup>13,14</sup> There is a similarity in opinion that the transfer of blastocysts or embryo to day 5 transfers produce fewer embryo transferred. It results in a higher implantation rate, and increases clinical

pregnancy rates.<sup>15</sup> This was in line with other studies which found that extending embryo culture to day 5 can be a better strategy for identifying and selecting groups of embryos with a higher overall probability of success for implantation.<sup>16</sup> Embryo implantation is a complex process. Improved clinical results have been seen with blastocyst transfer compared to cleavage phase embryos. Given the available evidence, improved results are seen after the 5th day embryo transfer.<sup>17</sup>

Table 1. Data embryo transfers on the 3rd and 5th day of IVF process with the success rate of pregnancy

Embryo Transfer 3 <sup>rd</sup> day or 5 <sup>th</sup> day	$\beta$ -hcg positive ( $\geq 25$ IU)	$\beta$ -hcg negative ( $\leq 25$ IU)	p
ET day 3	21(9.06)	39(16.8)	0.090
ET day 5	39(22.1)	40(22.7)	

Table 2. Data on pregnancy success rates and the stage of division in the embryo of the IVF process

Pregnancy	$\beta$ -hcg positive ( $\geq 25$ IU)	$\beta$ -hcg negative ( $\leq 25$ IU)	p
Blastosis	34(17.6)	36	0.298
Morula	2(0.05)	2(0.05)	
16 cells	3(0.06)	0(0)	
12 cells	9(1.73)	17(3.27)	
10 cells	1(0.01)	1(0.01)	
8 cells	9(1.67)	16(2.96)	

## CONCLUSION

It was found that embryo transfer on third and fifth day lead to the same rates of pregnancy success in IVF participants in Graha Amerta Hospital, Surabaya.

## ACKNOWLEDGMENT

We express our gratitude to the Department of Obstetrics and Gynecology, Faculty of Medicine, Universitas Airlangga, Dr. Soetomo Hospital, Surabaya and to the Infertility Clinic, Graha Amerta Hospital, Surabaya.

## REFERENCES

- World Health Organization (WHO). WHO manual for the standardized investigation and diagnosis of the infertile couple. Cambridge: Cambridge University Press; 2000.
- Van der Borgh M, Wyns C. (2018). Fertility and infertility: Definition and epidemiology. *Clinical Biochemistry*. 2018;62:2-10.
- Spitzer D, Haidbauer R, Corn C, et al. Effects of embryo transfer quality on pregnancy and live birth delivery rates. *Journal of Assisted Reproduction and Genetics*. 2011;29(2):131-5.
- Edwards RG, Brody SA. History and ethics of assisted human conception. In: Principles and practice of assisted human reproduction. Philadelphia: Saunders; 1995, p. 17-47.
- Hatırnaz Ş, Kanat Pektaş M. Day 3 embryo transfer versus day 5 blastocyst transfers: A prospective randomized controlled trial. *Turk J Obstet Gynecol*. 2017;14(2):82-8.
- Dahiya M, Rupani K, Yu S, et al. Embryo transfer day does not affect the initial maternal serum beta-hCG levels: A retrospective cohort study. *European Journal of Obstetrics & Gynecology and Reproductive Biology*. 2017;212:75-9.
- Papanikolaou. *Rbmojournal*; 2018 [cited 2018 Oct 18] Available from [https://www.rbmojournal.com/article/S1472-6483\(10\)60981-9/pdf](https://www.rbmojournal.com/article/S1472-6483(10)60981-9/pdf)
- Martins WP, Nastri CO, Rienzi L, et al. Blastocyst vs cleavage-stage embryo transfer: systematic review and meta-analysis of reproductive outcomes. *Ultrasound Obstet Gynecol*. 2017;49(5):583-91.
- Kaartinen N, Das P, Kananen K, et al. (2015). Can repeated IVF-ICSI-cycles be avoided by using blastocysts developing from poor-quality cleavage stage embryos? *Reproductive BioMedicine Online*. 2015;30(3):241-7.
- Lee C, Lee T, Huang C, et al. Detection of early cleavage embryos improves pregnancy and delivery rates of Day 3 embryo transfer during I in vitro fertilization. *Taiwanese Journal of Obstetrics and Gynecology*. 2016;55(4):558-62.
- Herbement C, Sarandi S, Boujenah J, et al. Should we consider day-2 and day-3 embryo morphology before day-5 transfer when blastocysts reach a similar good quality? *Reproductive BioMedicine Online*. 2017;35(5):521-8.
- Adamson G, Abusief M, Palao L, et al. (2016). Improved implantation rates of day 3 embryo transfers with the use of an automated time-lapse-enabled test to aid in embryo selection. *Fertility and Sterility*. 2016;105(2):369-375.e6.
- Kumbak B, Oral E, Karlikaya G, et al. Serum oestradiol and beta-HCG measurements after day 3 or 5 embryo transfers in interpreting pregnancy outcome. *Reprod Biomed Online*. 2006;13(4):459-64.
- Racowsky. *rbmonline.com*. [internet] *Rbmonline.com*. [cited 2018 Oct 18] Available at: <http://www.rbmonline.com/Article/807>
- Revelli A, Canosa S, Carosso A, et al. Impact of the addition of Early Embryo Viability Assessment to morphological evaluation on the accuracy of

- embryo selection on day 3 or day 5: a retrospective analysis. *J Ovarian Res.* 2019;12(1):73.
16. Mastenbroek S, van der Veen F, Aflatoonian A et al. Embryo selection in IVF. *Hum Reprod.* 2011;26(5):964-6.
  17. Tiegs A, Franasiak J. The embryo day 3 versus day 5 ET. *Encyclopedia of Reproduction.* 2018; p. 278-83.