

Incidence of treatment-independent spontaneous pregnancies in ART

Alhelou Y^{1,5}, AlShammeri DS², AlBlushi SA³, AlFarraj A⁴, Al Yami SA⁴, Al Badran AK⁴

¹Fakih IVF Fertility Center, Abu Dhabi, United Arab Emirates.

²Department of Obstetrics and Gynecology, College of Medicine, Imam Muhammad Ibn Saud Islamic University, Riyadh, Najd, Kingdom of Saudi Arabia

³Department of Radiology, Maternity and Children Hospital, Dammam, Eastern Region, Kingdom of Saudi Arabia

⁴Department of IVF, Maternity and Children Hospital, Dammam, Eastern Region, Kingdom of Saudi Arabia

⁵Department of ObGyn, Faculty of Medicine, University of Malaya, Kuala Lumpur, Malaysia

Abstract

Background

Chance spontaneous pregnancy (SP) is known to occur in ART patients during, after successful, or failed IVF treatment cycles. The objective of the present study is to report the authors' experience with SP, to undertake an overview of similar findings in the literature, and to calculate and determine the incidence of SP based on a larger data set from the literature.

Subjects and methods

A total of 231 patients with unexplained infertility who had failed IVF cycles were studied. We searched the literature for reports of spontaneous pregnancies in ART patients and compiled a total of 12 reports, including the present report. The incidence of SPs using a larger data set from the literature and a simple overview was performed.

Results

The rate of SP was 23.4% (54 cases) in failed ART cycles compared with 11.4 (nine cases) in the control group. We obtained 11 reports from the literature, which together with the authors' report, lent itself to calculate the overall percentage and incidence of SP in ART patients which was 13.5% (866/6429).

Discussion and Conclusion

The chances of spontaneous conception during, after successful, or failed IVF cycles occur in about 13.5% of ART patients but this is not representative of different forms of infertility because of the vastly varied etiologies of the condition. The actual incidence of SP for individual types of infertility can only be determined with data set with sufficient numbers of patients for each type of infertility. The occurrence of SPs has implications for the practice and counseling in ART.

Disclaimer: The authors have no conflicts of interest.

J Reprod Biotechnol Fertil 11:104-107

Correspondence: Y Alhelou; email: alhelou@yahoo.com

Compliance acknowledgment: This article was edited by the Australian Editorial Services (www.nativeenglisheditor.com)

Keywords: ART, IVF, Incidence, spontaneous pregnancy, treatment-independent.

Introduction

It is well-recognized that the etiologies for human infertility are varied and multifactorial. The treatment modality of in vitro fertilization and embryo transfer (IVF-ET) and related services collectively called assisted reproduction technology (ART) was developed for couples

who are unable to conceive naturally due to the various causative factors of infertility such as untreatable tubal factor, endometriosis, sperm-hostile cervical factor, male factor, unexplained infertility, and other relevant pathological conditions. ART is considered the final treatment

option for such patients. It is therefore quite intriguing when spontaneous pregnancy (SP) occurs in these categories of patients, which is usually completely unanticipated. Indeed, ART clinics appear to encounter on an almost regular basis patients that conceive spontaneously while under investigation, after failed ART treatment, or after the successful completion of treatment (Collins et al., 1983; Ben-Rafael et al., 1986; Haney et al., 1987; Roh et al., 1987; Correy et al., 1988; Harrison et al., 1995; Vardon et al., 1995; Matorras et al., 1996; Snick et al., 1997; Evers et al., 1998; Shimizu et al., 1999; Hennelly et al., 2000; Alhelou et al., 2003; Troude et al., 2012; Soave et al., 2012; Hanafiah et al., 2015; Tanacan and Beksac 2019).

The objective of the present study is to report our own experiences with SP and, to undertake an overview of similar findings in the literature (Ben-Rafael et al., 1986; Haney et al., 1987; Roh et al., 1987; Harrison et al., 1995; Vardon et al., 1995; Matorras et al., 1996; Evers et al., 1998; Shimizu et al., 1999; Hennelly et al., 2000; Alhelou et al., 2003; Troude et al., 2012; Hanafiah et al., 2015) and to determine the incidence of SP based on a larger data set.

Subjects and Methods

Spontaneous conception after failed IVF cycles in patients with unexplained infertility was investigated. The control group is coupled with unexplained infertility who did not undergo IVF, either because they wanted to conceive in natural ways or they could not afford IVF expenses. A total of 231 patients with unexplained infertility who had failed IVF cycles were studied. The control group was 79 patients with unexplained infertility who did not undergo IVF.

A literature search on reports of spontaneous pregnancies in IVF patients was performed using the Pubmed online resources.

Results

Case Studies on Spontaneous Pregnancies

The rate of spontaneous pregnancies was 23.4% (54 cases) in failed ART cycles compared with 11.4 (nine cases) in couples that have not undergone ART treatment. Women in the 2 years following the failed cycles. The mean age

was 31.1 versus 30.8 years in the control ($P < 0.05$), and the mean duration of infertility before IVF was 6.1 years.

Incidence of spontaneous pregnancies in IVF patients.

The Pubmed search identified 11 reports on SPs in IVF patients. The data set from 12 reports, including the present report, were compiled and utilized to calculate the incidence of SPs in IVF patients. The proportion of SPs in IVF patients due to various etiologies from the 12 individual reports included in this communication are shown in Table 1.

The combined data set of the 12 studies lent itself to calculate the overall percentage and incidence of SP in ART patients. The data from the 12 studies gave an incidence rate of 13.5% (866/6429) for SPs in IVF patients.

Discussion

The data accrued from the literature and the present study on SPs suggest its incidence to be in the vicinity of 13.5%. However, it is not possible to generalize about the incidence of SPs because the etiologies of infertility are multifactorial and varied. If taken individually, the incidence of SPs is much higher in some forms of infertility compared to, for instance, severe male factor infertility (Matorras et al., 1996). Overall based on the high volume of data on SPs from the literature demonstrate that about 1 in 7 to 8 (i.e 13.5%) patients could have a chance of SP, particularly those who are young, with shorter durations of infertility, women with endometriosis, unexplained infertility, and men with a mild male factor problem (Shimizu et al., 1999; Hennelly et al., 2000; Al Helou et al., 2003). There was a trend towards conception among those who had a shorter duration of infertility. Alhelou et al., 2003). A much larger data set is needed to determine the incidence of SPs in individual etiologies of infertility.

Most IVF patients are convinced they could only conceive through IVF/ICSI and that there is no other way to achieve parenthood. However, SPs puts this perception to question. It is obvious from available data, chance SPs can occur independently of treatment in those patients considered sub-fertile or infertile after

Table 1: Reports on Spontaneous Pregnancies

Authors	Spontaneous Pregnancies (all categories)		
	% Pregnancies	Nos. of Pregnancies	Total Cycles Nos.
Ben-Rafael et al., 1986	17.5	13	74
Haney et al. 1987	7.8	19	245
Roh et al. 1987	11.9	18	151
Harrison et al., 1995	11.7	78	662
Vardon et al., 1995	11.2	54	482
Motarras et al., 1996	3.2	9	285
Evers et al., 1998	5.5	76	1391
Shimizu et al., 1999	17.6	25	142
Henelly et al. 2000	20.7	106	513
Troude et al., 2012	19.3	411	2134
Hanafiah et al., 2015	2.5	3	119
This report, 2022	23.4	54	231
Total	13.5	866	6429

meticulous full infertility investigation and were told they have to undergo IVF treatment to become parents. The authors concur that the role of chance SP must be discussed with patients considering IVF treatment (Hennelly et al., 2000) because of its significant probability in 1 of 7 or 8 patients, and its definite occurrence.

Shimizu and coworkers suggested that IVF patients who intend to undergo additional IVF treatment cycles soon after a successful cycle should be counseled to wait two years before doing so if they are between the ages of 28 and 33 because 20–25% of them will have an SP during that time. On the contrary, resuming IVF therapy as soon as feasible is advised for women who are 34 years old and hoping to get pregnant again because the likelihood of future spontaneous conception is minimal (Shimizu et al., 1999). This is well documented since the probability of SP decreases with the increase in the age of the woman (cited in Troude et al., 2012).

What could have contributed to the occurrence of chance SPs? The objective of ART is to investigate thoroughly the cause(s) of infertility and to increase the quantity of retrievable preovulatory oocytes using a variety of techniques including invasive diagnostic

procedures. Maybe these procedures helped correct previously unknown abnormalities. It is suggested that a large proportion of workers believe diagnostic surgical, laparoscopic, and other manipulations may ameliorate anatomical defects or obstructions but this view is not shared by others (Roh et al., 1987). Ovarian stimulation is thought to correct a hitherto undetected ovulatory abnormality resulting in qualitatively enhanced ovulatory function which may facilitate SP. Therefore, it is assumed ovarian hyperstimulation may have a therapeutic effect on ovulation (Haney et al., 1987; Roh et al., 1987). Another crucial element of ART treatment is formal stress management. Effective stress management could, in part, be attributed to SPs (Harrison et al 1995; Soave et al., 2013). Extramatrimonial pregnancy does not appear to be the cause of SPs even in severe oligozoospermia (Matorras et al., 1996).

Conclusion

The chances of spontaneous conception during, after successful, or failed IVF cycles occur in about 13.5% of ART patients but this is not accurate because of the vastly varied etiologies of infertility. The actual incidence of SP for individual types of infertility can only be

determined with data set with sufficient numbers of patients for each type of infertility. The occurrence of SPs has implications for the practice and counseling in ART.

References

- Alhelou Y, Alkerenawi G, Abohamda T, Alhelou T. Spontaneous conception after failed IVF cycles in patients with unexplained infertility. P-379. Abstracts of the 19th Annual Meeting of the ESHRE, Madrid, Spain 2003.p. Human Reprod. xviii129
- Ben-Rafael Z, Mashiach S, Dor J, Rudak E, Goldman B. Treatment independent pregnancy after an in vitro fertilization and embryo transfer trial. *Fertil Steril* 1986;45:564–567.
- Collins JA, Wrixon W, Janes LB, Wilson EH: Treatment independent pregnancy among infertile couples. *N Engl J Med* 1983; 309:1201
- Correy JF, Watkins RA, Bradfield GF, Garner S, Watson S, Gray G. Spontaneous pregnancies and pregnancies as a result of treatment on an in vitro fertilization program terminating in ectopic pregnancies or spontaneous abortions. *Fertil Steril* 1988;50:85–88.
- Evers JL, de Haas HW, Land JA, Dumoulin JC, Dunselman GA. Treatment-independent pregnancy rate in patients with severe reproductive disorders. *Human Reprod.* 1998;13(5):1206–1209
- Hanafiah S, Idris SK, Tarmizi HA, Mahfudzah S, Ata'allah GA, Rashid MA, Razali N, Mat Adenan NA, Ali J. Possibility of spontaneous natural pregnancy of 2.5% after failed art treatment . Proceedings of the Malaysian Association of Clinical Embryologist Annual Conference, MACE2015, 17 October 2015, University of Malaya, Kuala Lumpur, Malaysia
- Haney AF, Hughes CL Jr, Whitesides DB, Dodson WC. Treatment independent, treatment-associated, and pregnancies after additional therapy in a program of in vitro fertilization and embryo transfer. *Fertil Steril* 1987;47:634–638.
- Harrison RF, Hennelly B, Woods T, Lowry K, Kondaveeti U, Barry-Kinsella C, Nargund G. Course and outcome of IVF pregnancies and spontaneous conceptions within an IVF setting. *Eur J Obstet Gynecol Reprod Biol.* 1995;59(2):175-182.
- Hennelly B, Harrison RF, Kelly J, Jacob S, Barrett T. Spontaneous conception after a successful attempt at in vitro fertilization/intracytoplasmic sperm injection. *Fertil Steril.* 2000;73(4):774-778.
- Evers JL, de Haas HW, Land JA, Dumoulin JC, Dunselman GA. Treatment-independent pregnancy rate in patients with severe reproductive disorders. *Human Reprod.* 1998;13(5):1206–1209
- Matorras R, Diez J, Corcóstegui B, de Terán GG, García JM, Pijoan JI, Rodríguez-Escudero FJ. Spontaneous pregnancy in couples waiting for artificial insemination donor because of severe male infertility. *Eur J Obstet Gynecol Reprod Biol.* 1996;70(2):175-178.
- Roh SI, Awadalla SG, Friedman CI, Park JM, Chin NO, Dodds WG, et al. al. In vitro fertilization and embryo transfer: treatment-dependent versus -independent pregnancies. *Fertil Steril* 1987;48:982–986.
- Shimizu Y, Kodama H, Fukuda J, Murata M, Kumagai J, Tanaka T. Spontaneous conception after the birth of infants conceived through in vitro fertilization treatment. *Fertil Steril.* 1999;71(1):35-39.
- Snick HK, Snick TS, Evers JL, Collins JA. The spontaneous pregnancy prognosis in untreated subfertile couples: the Walcheren primary care study. *Human Reprod.* 1997;12(7):1582-1588.
- Soave I, Lo Monte MR, Marci R. Spontaneous pregnancy and unexplained infertility: a gift with many whys. *N Am J Med Sci.* 2012;4(10):512-513.
- Tanacan A, Beksac MS. Spontaneous pregnancies in patients with at least one failed IVF cycle after the management of autoimmune disorders, hereditary thrombophilia, and methylation disorders. *JBRA Assisted Reproduction.* 2019;23(4):361.
- Troude P, Bailly E, Guibert J, Bouyer J, de la Rochebrochard E; DAIFI Group. Spontaneous pregnancies among couples previously treated by in vitro fertilization. *Fertil Steril* 2012;98:63 68.
- Vardon D, Burban C, Collomb J, Stolla V, Erny R. Spontaneous pregnancies in couples after failed or successful in vitro fertilization. *J Gynecol Obstet Biol Reprod.* 1995;24(8):811-815.