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ORIGINAL PAPER

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The Kind of Conception Affects the Kind of Cesarean Delivery in Primiparous Women

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ABSTRACT

Background: So far, multiple factors have been found to be related to the IVF procedure, the most prevalent being extremes of maternal age, infections, previous gynecological history, infertility and others. Although women achieve the coveted pregnancy with the development of IVF technology, the rapid increase contributes to the increase of primary cesarean sections rates. **Objective:** The aim of the study was to identify if the kind of conception affects the kind of cesarean delivery among primiparous women in Greece. **Methods:** This cross-sectional observational study took place from September 2019 to February 2020 at the University Hospital of Larisa in Greece. One hundred and sixty-two primiparous women who underwent a cesarean section (c-section) after IVF (n=27) and natural conception (n=135) participated in the study. **Results:** The mean age of the IVF and natural conception groups were 36.22 and 31.08 years, respectively. Nineteen (70.4%) women of the IVF group had a previous medical or gynecological history in contrast to 48 (35.6%) women of the natural conception group. Only 55.6% of the IVF group had a full-term pregnancy unlike 88.1% of women in the natural conception group. An elective c-section was performed in 18 (66.7%) of the women who conceived after IVF, as opposed to 45 (33.3%) of the women who conceived naturally. **Conclusion:** This cross-sectional study showed that IVF conception was associated with high rates of elective cesarean section as opposed to women with natural conception. The causes of c-sections must be evidence based because the primary cesarean delivery is a major factor contributing to increased c-section rates.

Keywords: natural conception, c-section, in vitro fertilization, IVF conception, elective cesarean

section, emergency cesarean section.

1. BACKGROUND

Techniques that involve the manipulation of oocytes outside the body are called assisted reproductive technology, with in vitro fertilization (IVF) as the most common form (1). Since the first (IVF) baby was born in 1978, IVF methods have increased dramatically and now account for 1.6% and 4.5% of all live births in the United States and Europe respectively (2). Originally yielding single-digit success rates, IVF nowadays is successful in nearly 50% of the cases in women younger than 35 years old (3).

Approximately 25% to 35% of infertile women are found to have previous gynecological history such as infection or endometriosis (4) and the rehabilitation of the problem with laparoscopic surgery shows the importance of a healthy pelvic system in female fertility (1). When intrauterine fertilization fails, IVF can also increase pregnancy rates in couples where the male partner has a low number of motile sperm. Furthermore, women with a reduced number of oocytes or without oocytes can also get pregnant with donor oocytes or donor embryos after IVF procedure (5).

Women after IVF conception are a special population of pregnant women. Most of the time, these women are older than women conceiving naturally, due to many years of infertility. Actually, advanced age is a risk factor for female infertility as well as, pregnancy loss, fetal anomalies, stillbirth, and obstetric complications (6). The intentional delay in pregnancy facilitated by the availability of effective contraception, can be attributed to increasing

educational opportunities often resulting in late marriages (7). However, the overall success of human reproduction is highly dependent upon maternal age. The main reasons for age-related infertility include reduced ovarian reserve as well as, a possibly decreased mitochondrial activity (8, 9).

There is a relationship between the women's health history and infertility. For example, thyroid diseases (10), multiple sclerosis (11), diabetes (12) and metabolic syndrome (13) can be causes of infertility. More specifically, the polycystic ovary syndrome is one of the most common reproductive endocrinological disorders in women, affecting about 15% of the general population and is associated with the metabolic syndrome. Evidence has shown that insulin resistance plays an important role in pathophysiology of polycystic ovary syndrome (13), while the compensatory hyperinsulinemia is also a key factor in the evolution of metabolic syndrome (14).

Furthermore, complications during pregnancy are more common in women after IVF conception than women who conceived naturally (15). It is already known that placenta abnormalities (16,17), and especially placenta accreta, which has a catastrophic effect on obstetrics, are associated with IVF pregnancies (18). Placenta abnormalities are usually associated with massive postpartum hemorrhages and have become the major indicator for emergent peripartum hysterectomy (19, 20). Bleeding and spontaneous abortion are also very common in the first trimester of pregnancies after IVF conception and, to some extent, this may be due to higher aneuploidy rates related to the advanced age of both parents (21, 22). A study of Szymanska M et al., showed high percentages of preeclampsia in women with IVF conception and diabetes in a small number of patients (23). Nevertheless, Watanabe et al., (24) indicated that the relationship between preeclampsia and IVF may be confounded by unmeasured factors.

Additionally, IVF has involved the transfer of multiple embryos, in order to increase the chance of a successful pregnancy outcome, that often results in multiple pregnancies and high-risk pregnancies (25). However, while a single embryo transfer reduces the risk of multiple gestations, multiple studies have shown that single infants conceived after IVF, whether after a multiple or a single embryo transfer, are at higher risk of preterm birth than naturally conceived singletons (26, 27, 28, 29).

In view of the above, we observe that, although IVF may help infertile couples to have children, it presents a major public health problem because of the associations with unfavorable birth outcomes such as prematurity, and complications during pregnancy (30, 28). According to this point of view, pregnancies conceived after IVF procedure, may be considered as "precious pregnancies"(31) therefore; the IVF also determines, to a large extent, the kind of delivery. Many studies have shown that the c-section rates are significantly higher after IVF than after natural conception (26, 32, 33) and this practice is often based on maternal desire and obstetricians decision (31). Indeed, although the elective cesarean section (ELCS) is preferred by obstetricians (32), emergency cesarean sections (EMCS) are also very common after IVF due to many complications during pregnancy (34).

Although there is no evidence that the high c-section rates reduced maternal-child perinatal morbidity and mortality, c-sections have been increasing both in high and low income countries (35). An overall of 29.7 (21.1%) million deliveries by c- section were performed in 2015, almost doubling the rate of 2000 (12.1%), while it is estimated that 6.2 million c-sections were performed without medical reason each year worldwide (36). The primary c-section is a major factor of increasing c-section rates since it carries a risk of repeating this kind of delivery in future pregnancies due to the fear of uterine scar (37, 38), justifying the Gragin's dictum "once a cesarean always a cesarean " (39).

2. OBJECTIVE

The aim of the study was to identify if the kind of conception affects the kind of cesarean delivery among primiparous women in Greece.

3. MATERIAL AND METHODS

Participants

This cross- sectional study took place from July 2019 to February 2020 at the Obstetrics Clinic of the University Hospital of Larisa in Greece. It was approved by the University Hospital Ethics Committee. Approval Number: 18838/08-05-2019.

During the research period 633 births took place. Of these, 268 (42%) involved vaginal deliveries and 365 (58%) c-sections. The c-sections consisted of 203 (64%) women with previous c- section and 162 (44.4%), who underwent a primary cesarean delivery (Figure 1). In order to have a sample that would allow us to fulfill the aim of this study, we selected women with primary c-section. This sample was divided into two different groups; one group of 135 women with natural conception and one group of 27 women after IVF conception (Figure 2). All women had a medical surveillance dossier from which the demographics and medical data were obtained.

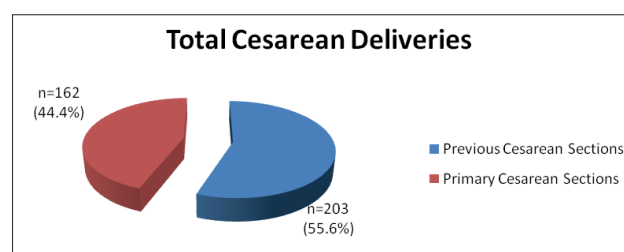


Figure 1. The proportion of previous and primaries c-sections in the total number of births by cesarean delivery

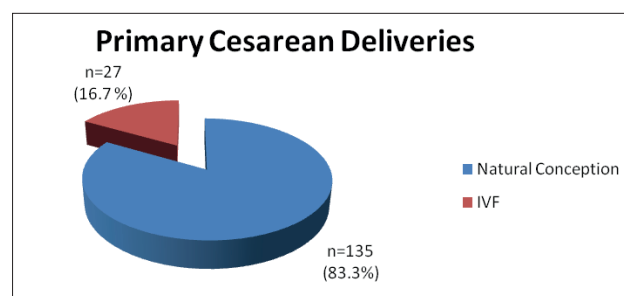


Figure 2. The proportion of natural conception and IVF in the total number of births by primary c-section

	Kind of conception	N	Mean	Mean Rank	Mann-Whitney U	p-value
Age	Normal	135	31.80	75.71	1041	<0.001
	IVF	27	36.22	110.44		

Table 1. Mann-Whitney test for the evaluation of the relationship between kind of conception and age.

Data and Measures

The medical and demographic data were collected in the 2nd day after childbirth, which coincides with the recovery of the women after surgery.

Socio-Demographic Questionnaire

The research-made screening form included items on demographic, social, medical (obstetric neonatal) and mental characteristics of the participants.

Medical Records

Data were collected from the women's medical records (which are paper-based in Greece), including information about the mothers' health before, during, and after the surgery. More specifically, the medical, gynecological and mental history and the pathology of gestation were recorded, as well as the type of conception, the causes that led to EMCS or ELCS and any postoperative complications. The combination of questionnaire and medical record was used to better detect information about the women's socioeconomic status and health level.

Statistical Analysis

For the comparison of proportions, Mann-Whitney U test and chi-square and Fisher's exact tests were used. A logistic regression analysis was not applied since IVF group was only 27 women. All statistic tests were two-tailed, with a significant set at $p < 0.05$. All statistical analyses were performed with SPSS 22.0 for Windows (SPSS; Chicago, IL, USA).

4. RESULTS

A cross-sectional observation study was conducted with a sample of 162 primiparous women after c-section, who were divided into a group of a) 135 women who conceived through a natural process (83.4%); and b) 27 women who conceived through an IVF process (16.6%) (Figure 2). A chi-square test and Fischer's exact test were used to compare proportions of normal conception and IVF conception with other variables on a nominal and ordinal scale. The influence of maternal age to the type of conception was examined via a Mann-Whitney U test (Table 1). Differences were considered to be statistically significant at a p-value of 0.05. The analysis shows that the mean age (36.22) of the mothers after IVF conception was statistically significantly higher than the mean age (31.80) of the mothers with natural conception ($p < 0.001$) (Table 1).

The socio-demographic, pregnancy and delivery characteristics are shown in Table 2. The analysis showed that variables such as family status ($p = 0.324$), financial status ($p = 0.809$), educational level ($p = 0.563$), occupation ($p = 0.423$), nationality ($p = 0.802$) and minority ($p = 0.842$) do not appear to be statistically significant between the two groups. On the contrary, statistically significant differences were found between the two groups concerning the patho-

logical health history ($p = 0.001$), the duration of pregnancy (the weeks of gestation age) ($p = 0.001$), the type of c-section ($p = 0.001$), the causes of c-section ($p < 0.001$), and the admission of a neonate in NICU ($p = 0.001$). More specifically, women with pathological health history (diabetes, autoimmune and gynecological problems), prematurity (gestation age < 37 weeks), elective c-section, the use of IVF procedure as a cause of c-section and admission in NICU due to prematurity seem to have a higher proportion in the group of women after IVF conception in relation to the group of women who conceived through a natural process (Table 2).

5. DISCUSSION

This is the first time that maternal and perinatal variables are researched relating to the kind of conception (natural conception or after IVF procedures) in the case of primiparous women who had given birth with c-section. According to Table 2, apart from the maternal age, there are no statistically significant differences in the demographic characteristics between the 2 groups of women. The above findings show that in public Greek hospitals, the socio-economic advantage does not apply to infertile couples who choose the IVF procedure as in other European countries (40).

It has long been clear that the maternal age has been associated with pathology of gestation such as diabetes, preeclampsia, infections, hormonal disorder, placental and myometrial vascular lesions, but also with burdened pathological situations during pregnancy (17, 41). Our results show that women who had conceived with IVF procedures are of a higher mean age than the women who conceived naturally ($p < 0.001$). In the female fetus, the proliferation of germ cells stops at about 20 weeks, resulting in women being born with a defined number of primordial follicles. At birth, the female neonate has approximately 5 million primordial follicles that are reduced to about 500,000 during menstruation. With each menstrual cycle, follicular depletion continues, with a decline to approximately 25,000 at the age of 37 and 1000 near menopause. The decline usually begins at age 32 with a dramatic drop after age 37 (7). So, increased maternal age is related to conception with IVF procedures, a result that has been identified in other studies (41, 42, 8). This finding is useful for the development of reproductive policies as we know that the mean age of women in Europe giving birth to their first child has gradually increased from 28.7 in 2013 to 29.1 in 2017. Also, Greece is one of the countries with the highest mean age at birth of first child in Europe (43).

Our findings showed that only 55.6% of IVF women had a full-term pregnancy, as opposed to 88.1% of women of the natural conception group. Due to the effects of this phenomenon, 22.2% of the neonates of IVF mothers were

		The Kind of Conception		χ^2 value	p-value			
		Natural (N=135) N (%)	IVF (N=27) N (%)					
Family status	Single	1 (0.7%)	0 (0%)	5.648	0.324*			
	In relationship	7 (5.2%)	2 (7.4%)					
	Married	126 (93.3%)	24 (88.9%)					
	Divorced	0 (0%)	1 (3.7%)					
	Engaged	1 (0.7%)	0 (0%)					
Educational level	Primary school	6 (4.4%)	1 (3.7%)	3.154	0.563*			
	Junior/ High school	6 (4.4%)	3 (11.1%)					
	Senior High school	57 (42.2%)	12 (44.4%)					
	University	55 (40.7%)	8 (29.6%)					
	Msc	10 (7.4%)	3 (11.1%)					
	PhD	1 (0.7%)	0 (0%)					
Occupation	Public/private sector	44 (32.6%)	13 (48.1%)	4.942	0.423			
	Freelance	26 (19.3%)	5 (18.5%)					
	Health care professional	10 (7.4%)	1 (3.7%)					
	Educators	13 (9.6%)	1 (3.7%)					
	Household	24 (17.8%)	6 (22.2%)					
	Unemployed	18 (13.3%)	1 (3.7%)					
	Financial status	Low	27 (20%)			4 (14.8%)	1.307	0.809*
Middle	104 (77%)	23 (85.2%)						
High	4 (3%)	0 (0%)						
Nationality	Greek	123 (91.1%)	25 (92.6%)	0.063	0.802			
	Other	12 (8.9%)	2 (7.4%)					
Minority	No	131 (97%)	26 (96.3%)	0.041	0.842*			
	Yes	4 (3%)	1 (3.7%)					
Pathological health history	No	87 (64.4%)	8 (29.6%)	11.245	0.001			
	Yes	48 (35.6%)	19 (70.4%)					
Complications during pregnancy	No	86 (63.7%)	15 (55.6%)	8.970	0.120*			
	Placenta location problems	8 (5.9%)	1 (3.7%)					
	Placenta insufficiency	20 (14.8%)	7 (25.9%)					
	Infection	4 (3%)	1 (3.7%)					
	Diabetes	16 (11.9%)	1 (3.7%)					
	Cervical insufficiency/Premature contractions	1 (0.7%)	2 (7.4%)					
Duration of pregnancy (the gestation weeks)	37 + (Fullterm).	119 (88.1%)	15 (55.6%)	16.754	0.001*			
	32-36+6 (late preterm)	13 (9.6%)	10 (37%)					
	22- 27.6 (extreme preterm)	3 (2.2%)	2 (7.4%)					
Type of c-section	Emergency	90 (66.7%)	9 (33.3%)	10.519	0.001			
	Elective	45 (33.3%)	18 (66.7%)					
Causes of c-section	IVF	0 (0%)	12 (44.4%)	124.223	<0.001			
	Twins gestation	3 (2.2%)	1 (3.7%)					
	IVF and twins' gestation	0 (0%)	9 (33.3%)					
	Abnormal fetal position	38 (28.1%)	1 (3.7%)					
	Placenta location problem/ bleeding	8 (5.9%)	0 (0%)					
	Abnormal heart rate/ abnormal NST	26 (19.3%)	1 (3.7%)					
	Failure of labor to progress	27 (20%)	0 (0%)					
	Mothers desire	12 (8.9%)	0 (0%)					
	Medical history	12 (8.9%)	1 (3.7%)					
	Preeclampsia	9 (6.7%)	2 (7.4%)					
	Complications after c-section	No	124 (91.9%)			23 (85.2%)	1.190	0.275
		Yes	11 (8.1%)			4 (14.8%)		
	Admission in NICU	No	108 (80%)			18 (66.7%)	19.562	0.001
Perinatal stress. Breathing disorder		21 (15.6%)	1 (3.7%)					
Infection		2 (1.5%)	2 (7.4%)					
Prematurity		4 (3%)	6 (22.2%)					

*Fisher's exact test; p<0.05.

Table 2. Relation between the kind of conceptions and the socio-demographic pregnancy and delivery characteristics

admitted to the NICU, as a result of prematurity, while only 3% of neonates after natural conception were born prematurely and admitted to the NICU. A meta-analysis published by Cavoretto, P et al., in 2017 (44), showed an increased risk of preterm birth, by approximately 80%. One of the main causes reported in this study is the type of infertility treatment and based on this finding; the authors suggest that infertility itself is a risk factor for preterm birth.

In this study, the pathological health history was more common in the IVF group (70.4%) compared to the natural conception group (35.6%) ($p=0.001$). This is a result that has also been recognized in other studies (45-48). Pathological conditions, such as polycystic ovary syndrome, which represents 80% of anovulatory infertility cases, are associated with the IVF procedure (49, 50).

Traditionally, IVF has involved the transfer of multiple embryos in order to maximize the possibility of a live birth; however, as IVF rates increase over time, the possibilities of multiple pregnancies increase respectively (25). Nevertheless, in our results twin gestations were more common among women with IVF conception and constitute one of the most important causes of c-section in Greece. Furthermore, the option of c-section for the group of IVF, and specifically of a scheduled one, reveals that both women and their gynecologists are reluctant to accept the risk of vaginal delivery (51, 52).

Another finding of our study is that women after IVF conception were more likely to undergo an ELCS, in contrast to women with natural conception who undergo more often an EMCS. This phenomenon explains the probability of the fear of the obstetricians about the outcome of an IVF pregnancy (53), as well as the view of some women who may perceive cesarean delivery to be safer for their babies than vaginal birth (54). It seems that IVF procedure is a stressful event for the affected women who may become pregnant after several failed attempts, they are older, and they are more at risk for complications during pregnancy. However, every painful IVF procedure entails daily injections of hormones and great expenditure in time, energy, and money. All these stressful factors could play a role in the decision of mothers and doctors to plan an ELCS at a time convenient for both of them.

In fact, an IVF pregnancy is no different from a natural one. However, the above factors, appear to be causes for c-section worldwide (28) and contributes to the increase of c-section rates globally. C-section can have immediate and long-term complications for the mother and the child (55). Nevertheless, the indications for c-section should be evidence-based only. That way, vaginal delivery will be supported.

Strengths and limitations

The present study has some limitations. One of them is the small sample size that prevented us from using logistic regression for the statistical analysis. Moreover, the IVF factor as a cause for c-section was so strong that overshadowed other factors that could lead to a c-section.

This is the first time, that a study researched mothers' characteristics, pregnancy and delivery variables in relation with the kind of conception (natural conception or after IVF procedures) in the case of primiparous women who

had given birth with c-section. Another strong points of the article is that the study was conducted at a university hospital that covers a large health district and provides IVF services.

6. CONCLUSION

This study documented that the type of conception is related to the kind of c-section. As we showed, women with IVF were more likely to have an ELCS compared to those who conceived naturally. Furthermore, the IVF group is of a higher mean age than the natural conception group, more burdensome health history and less likely to have a full-term pregnancy. This research confirms findings which suggest that the population of women who conceive after an IVF is different from the population of women who conceive naturally, and so, the IVF population deserves a closer dedicated midwifery and obstetrician care and follow-up. However, considering the short-term and long-term effects of c-section on the mother's and child's health, health policies related to the reduction of primary c-sections should be implemented.

- **Patient Consent Form:** All participants were informed about subject of the study.
- **Authors contribution:** E.A; E.O; M.I.; A.S; E.P; N.R.; G.I., and M.D contributed to the design and methodology and data analysis of the research. E.A conceived and designed the study and prepared the manuscript. All authors equally contributed to this manuscript. All authors have read and agreed to the published version of the manuscript.
- **Conflict of interest:** There are no conflicts of interest.
- **Financial support and sponsorship:** Nil.

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