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Maternal Fertility Status and Infant Outcomes: The Erebouni Medical Center Study of Assisted Reproductive Technology

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Introduction

The adoption of Assisted Reproductive Technology (ART) is witnessing a global surge. Current estimates indicate that approximately two percent of births across various countries are the outcome of ART interventions, and this percentage is projected to escalate in the upcoming years [4, 7].

Multiple research studies have highlighted that women undergoing Assisted Reproductive Technology (ART), particularly in-vitro fertilization (IVF), face an elevated susceptibility to maternal and neonatal complications when compared to their non-ART counterparts [1, 3, 5, 6, 8]. Conditions such as hypertensive disorders of pregnancy, gestational diabetes, low birth weight, preterm delivery, and placental complications have all been linked with subfertility and the utilization of IVF procedures [2]. Nevertheless, the primary drive behind these findings remains uncertain, as it remains to be determined whether these outcomes stem from the underlying infertility issues or from adverse effects resulting from infertility treatments or delivery methods.

Material and Methods

Study population and data collection.

This study represents a solitary-center case–control investigation carried out at Erebouni Medical Center, encompassing a cohort of 346 women over the period from January 2018 to December 2020. Within this timeframe, the study cohort consisted of women aged 16–51 years who underwent controlled ovarian hyperstimulation in conjunction with embryo transfer.

Pregnancies were meticulously monitored within the fertility unit until reaching a gestational age of 6–8 weeks, following which they were transferred to an outpatient clinic for continued oversight. Pertinent labor-related information was

gathered from the electronic medical records archived at Erebouni Medical Center. Notably, instances of miscarriage, ectopic pregnancy, as well as deliveries or patients with unavailable obstetric data were excluded from the study's analysis.

A control group was established comprising women who achieved conception through natural means. To ensure comparability, we conducted a matching process based on age and parity. The control group was also subject to parallel exclusion criteria.

Comprehensive data encompassing general medical history, pregnancy progression, labor, and delivery particulars, as well as outcomes were meticulously collected. Maternal and neonatal information was obtained from a computerized database, which undergoes continuous updates and validation processes for data related to admission, labor, and postpartum progress. Maternal general and obstetric data comprised essential information such as age, gravidity, parity, history of previous miscarriages and ectopic pregnancies, past vaginal and cesarean deliveries, pre-gestational and gestational diabetes mellitus, hypertensive disorders during pregnancy, and gestational age at delivery (measured in weeks).

Statistical analysis

Testing the association between two categorical variables was carried out using either the Chi-Square test or the Fisher's exact test, as indicated. The Fisher's exact test was applied in analyses of small samples, when more than 20% of cells have expected frequencies of less than 5. Quantitative variables were compared using the student's t-test for the two independent groups or the Mann–Whitney U-test. The student's t-test was used for normally distributed parameters, while the Mann–Whitney U-test was done for non-normally distributed parameters samples.

Univariate analysis was performed to identify factors associated with spontaneous vaginal delivery. Descriptive univariate analyses were performed accordingly. Variables found significantly associated with the dependent variable of spontaneous vaginal delivery in the univariate analysis, were entered into the multivariate logistic regression model. The significance of each variable and the adjusted Odds Ratio and 95% confidence interval (OR, 95% CI) were calculated. A p-value of < 0.05 was considered statistically significant for all comparisons.

Results and Discussion

Throughout the study period, 346 women with an age range of 16 to 51 years (mean age: 30.0±0.2 years), who had undergone in vitro fertilization (IVF) and achieved clinical pregnancy, were included in the analysis. These participants were categorized into three distinct groups based on their age:

Group 1: Pregnant women below 30 years old (n=171, mean age: 26.0±0.2 years). Among this group, 33 (19%) experienced twin pregnancies, and 4 (2.3%) had triple pregnancies.

Group 2: Pregnant women between 30 and 35 years old (n=108, mean age: 32.1±0.3 years). Among them, 26 (23.6%) were carrying twin pregnancies, and one (0.9%) was identified with a triple pregnancy.

Group 3: Pregnant women aged 36 years and above (n=61, mean age: 39.0±0.4 years). Within this category, eight (13.1%) women experienced twin pregnancies.

Table 1

Demographic Overview of Pregnant Women and Births at Erebouni Medical Center (2018–2020)

Year	Total Pregnant Women	Total Births	Premature Births	IVF-Conceived Births
2018	6082	4445 (73%)*	510	116*
2019	6642	4812 (72.4%)*	577	114*
2020	6557	5115 (78%)*	626	117*
Total	19281	14372 (74.5%)*	1713 (8.9%)	347 (1.8%)*

Statistical significance was defined as P<0.05 (; Significant)*

Throughout the research period, a total of 19 281 pregnant women were recorded at Erebouni Medical Center, with the number of births totaling to 14 372 (74.5%), of which 1713 (8.9%) were classified as premature births. It is noteworthy that during the study period, numbers of pregnant women increased, and in this regard, live births. Notably, a subset of 1.8% of these births was attributed to individuals who had undergone conception via the IVF pathway.

According to the obtained data, 12.4% of the pregnant women who applied to the Erebouni medical center belong to the 36+ age group, 31.3% to the 30-35 and 56.3% to the 36+ age groups. The age composition of pregnant women with IVF was comparable with the presented general picture with a slight difference: 18% belong to 36+; 32% - 30-35 and 50% - 36+ age groups.

Male factor infertility emerged as the predominant diagnosis, accounting for 59.6% of cases, followed by combined female and male etiology at 6.9%. Ovulation disorders constituted 10.3%, unexplained infertility stood at 4.6%, and endometriosis comprised 3.5% of diagnoses.

The comparison between the study groups revealed no discernible differences in maternal characteristics, encompassing factors such as prior miscarriages, vaginal births, and caesarean sections, as detailed in Table 2.

In the subset of pregnant women who underwent IVF, pre-eclampsia and complicated somatic anamnesis exhibited the highest occurrence within the 36+ age group, representing 9.8% and 17.5% respectively.

Table 2

Clinical Characteristics of IVF Pregnant Women

Parameters	< 30 n=171		30-35 n=109		36+ n=61		P
	abs.	%	abs.	%	abs.	%	
Gravidity							*
1	110	64.3	75	68.8	32	52.5	
2 or more	61	35.7	34	31.2	29	47.5	
Parity							*
0	94	55	56	51.4	44	72.1	
1	45	26	22	20.2	10	16.4	
2 or more	32	19	31	28.4	7	11.5	
Previous Vaginal Deliveries	11	6.4	6	5.5	5	3.8	*
Previous Cesarean Deliveries	2	1.2	0	0	1	1.6	*
Preeclampsia	2	1.2	6	5.5	6	9.8	*
Complicated gynecological anamnesis	125	73	80	73.3	45	73.4	*
Complicated somatic anamnesis	7	11.5	14	12.8	30	17.5	*

Statistical significance was defined as P<0.05 (; Significant)*

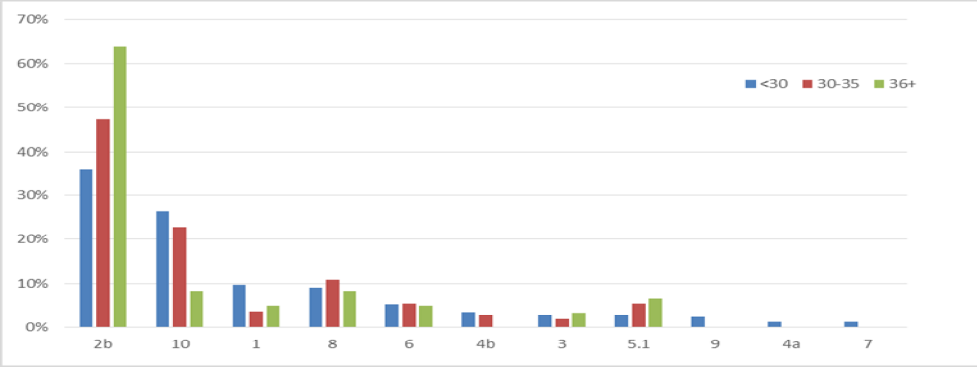

Fig. 1. Distribution of IVF Pregnancies According to Robson's Classification

In our research, we observed distinctive patterns among pregnant women who underwent IVF treatment. The prevalent Robson classification groups within this cohort were 2b, 10, and 8 (Fig.1). Notably, a considerable proportion of women in these groups underwent cesarean section deliveries.

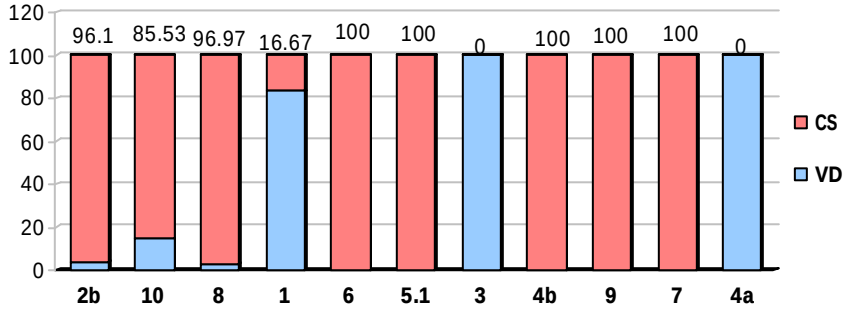

Fig. 2. Distribution of IVF pregnancies by Robson's group and mode of delivery

Conversely, pregnant women who underwent IVF and experienced natural vaginal delivery were primarily associated with groups 3, 4a, and 1 according to the Robson classification. This classification framework provided valuable insights into the delivery patterns among the subset of pregnant women who underwent IVF in our study.

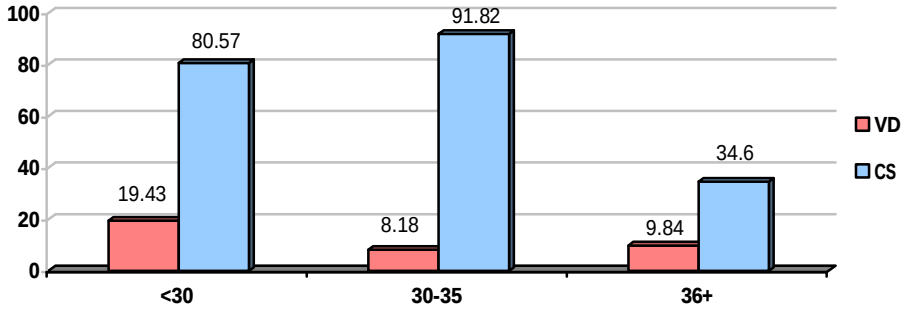

Fig. 3. Distribution of IVF pregnancies by age and mode of delivery

Based on the data we gathered, the highest count of caesarean sections was conducted among patients aged 30-35 and 36+ years (see Fig. 3). Simultaneously, the prevalence of preterm births was notable in the age group of 36+ years (34.6%), compare with the patients aged 30-35 (27.27%) and <30 (25.71%). The single-ton pregnancies were most frequent within the 36+ age group (as depicted in Fig. 4).

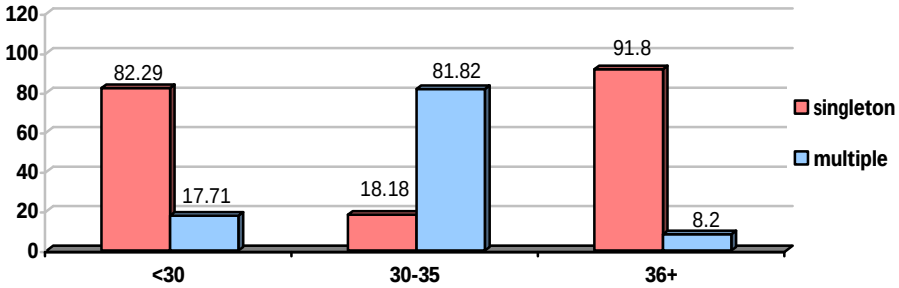

Fig. 4. Distribution of IVF pregnancies by age and number of fetuses

The primary contributors to the frequency of cesarean sections between 2018 and 2020 in our research were identified as groups 6, 5.1, 4b, 9, 7, 2b, and 10 according to the Robson classification. The group that consistently had the highest rate of operative deliveries were women with previous uterine scars, with 77.6% of them undergoing repeat operations. Notably, every fourth abdominal delivery at the Erebouni medical center occurred in cases where a uterine scar was present. While adopting a personalized approach for patients within these groups is expected to reduce the proportion of abdominal births, it is important to emphasize that regardless of protocol differences, the primary focus for preventing an increase in cesarean section rates lies in effective labor management and prevention of primary cesarean surgeries.

The second highest incidence of cesarean sections was observed in singleton pregnancies with pelvic presentations (over 23%) and transverse presentations (over 5.7%). This consistent high frequency can be attributed to the rising rate of scheduled births at the perinatal center each year due to its specific characteristics. The main reasons for preinduction in such cases include decompensated diabetes mellitus, post-term pregnancies, and early delivery due to pre-eclampsia (refer to Fig. 1).

Frequently, the rise in cesarean deliveries within this group can be linked to challenges in implementing pre-induction and labor induction protocols. A persistent and increasing rate of cesarean sections is observed in patients with preterm births and singleton pregnancies [5]. The elevated incidence of cesarean sections in the group 10 is justified by modern obstetric practices. Reducing the percentage of cesarean deliveries in this group necessitates comprehensive preconception preparation, particularly in high-risk groups.

Ranking fourth in terms of its impact on the distribution of operative deliveries, the 1st group initially appeared well-suited for vaginal births. Upon classifying instances of emergency cesarean sections within this group, we identified fetal distress and labor anomalies, including abnormal preliminary periods preceding labor, as the main indications for surgery. These factors can be managed effectively through adequate assessment of perinatal risk factors and prudent monitoring of fetal well-being.

Study Limitations

While our study provides valuable insights into childbirth outcomes in women after in vitro fertilization (IVF) and the associated risk of maternal and infant complications based on delivery method, several limitations should be acknowledged.

Firstly, the study was conducted at a single center, Erebouni Medical Center, which may limit the generalizability of our findings to broader populations. Variations in patient demographics, healthcare practices, and access to assisted reproductive technology services across different centers could influence the outcomes observed in our study.

Secondly, the sample size of 346 women, while sufficient for our analyses, may be considered relatively small in the context of epidemiological studies. As a result, there may be limitations in the statistical power to detect smaller effect sizes or to generalize findings to larger populations.

Thirdly, our study relied on retrospective data collection from electronic medical records, which may introduce inherent biases or inaccuracies. Despite our efforts to ensure data accuracy and completeness, the possibility of missing or incomplete data cannot be entirely ruled out.

Furthermore, while we aimed to control confounding variables through matching and statistical adjustments, the presence of unmeasured or residual confounders may still influence the observed associations between maternal fertility status, delivery methods, and infant outcomes.

Lastly, the use of Robson classification as a tool for evaluating cesarean section rates, while valuable, may have limitations in its application across different healthcare settings. The classification system may not fully capture all relevant factors influencing cesarean section rates, and its interpretation may vary among institutions.

Acknowledging these limitations is crucial for interpreting our findings accurately and understanding the scope and potential implications of our study within the context of assisted reproductive technology and childbirth outcomes research. Future studies with larger sample sizes, multi-center designs, and prospective data collection methods are warranted to validate our findings and address these limitations comprehensively.

Conclusion

In summary, our study provides valuable insights into childbirth outcomes following in vitro fertilization (IVF) and highlights the importance of personalized care in managing pregnancies after assisted reproductive technology. Despite limitations, our findings underscore the need for further research to validate and expand upon our observations. By emphasizing evidence-based decision-making and multidisciplinary collaboration, we can optimize maternal and neonatal outcomes for women undergoing IVF and advance clinical practice in this field.

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Статус фертильности матери и исходы для новорожденных: исследование вспомогательных репродуктивных технологий в Медицинском центре «Эребуни»

Н.Н. Гукасян

После экстракорпорального оплодотворения (ЭКО) выбор наиболее подходящего метода родоразрешения остается крайне важным. Естественные роды часто связаны с меньшим количеством осложнений как для матери, так и для новорожденного; однако в отдельных случаях кесарево сечение (КС) необходимо для достижения оптимальных результатов.

Наша цель – оценить исходы родов у женщин после ЭКО и проанализировать материнские и неонатальные осложнения в зависимости от способа родоразрешения.

В Медицинском центре «Эребуни» с 2018 по 2020 годы было проведено одномоментное исследование «случай-контроль», включившее 346 женщин в возрасте от 16 до 51 года, забеременевших с помощью ЭКО. Участницы включали одноплодные и многоплодные беременности, распределенные по возрасту матери и количеству плодов. Контрольная группа была сформирована в соотношении 1:2, сопоставленная по возрасту матери и паритету. Демографические характеристики, медицинская история, осложнения, связанные с беременностью, и исходы для матери и новорожденного были сопоставлены между группами.

Среди беременных после ЭКО 12,4% женщин были в возрасте ≥36 лет, 31,3% – 30–35 лет и 56,3% – <30 лет. Основной причиной бесплодия был мужской фактор (59,6%), за которым следовали сочетанное женское и мужское бесплодие (6,9%), овуляторные нарушения (10,3%), бесплодие неясного генеза (4,6%) и эндометриоз (3,5%). Классификация Робсона выявила группы 6; 5,1; 4b; 9; 7; 2b и 10 как основные факторы, влияющие на частоту КС. Характеристики и осложнения у женщин с ЭКО были сопоставимы с контрольной группой.

Классификация Робсона является ценным инструментом для оценки исходов родов и выявления направлений для улучшения. Несмотря на достижения в области ЭКО, частота КС остается высокой, подчеркивая необходимость индивидуального подхода к выбору метода родоразрешения для оптимизации исходов у матери и новорожденного.

Մոր վերարտադրողականության կարգավիճակը և նորածնային ելքերը. օժանդակ վերարտադրողական տեխնոլոգիաների հետազոտություն «Էրեբունի» բժշկական կենտրոնում

Ն.Ն. Ղուկասյան

Օժանդակ վերարտադրողական տեխնոլոգիաներով (IVF) բեղմնավորումից հետո ծննդաբերության ամենահարմար մեթոդի ընտրությունը մնում է վճռորոշ: Բնական ծննդաբերությունը հաճախ կապված է ավելի քիչ բարդությունների հետ ինչպես մոր, այնպես էլ նորածնի համար, սակայն որոշ դեպքերում կեսարյան հատումը (ԿՀ) անհրաժեշտ է՝ օպտիմալ արդյունքներ ապահովելու համար: Մեր նպատակն է գնահատել IVF-ից հետո կանանց մոտ ծննդաբերության ելքերը և վերլուծել մայրական և նորածնային բարդությունները՝ ելնելով ծննդաբերության եղանակներից: «Էրեբունի» բժշկական կենտրոնում 2018–2020 թթ. կատարվել է մեկ կենտրոնում իրականացված դեպք-վերահսկման հետազոտություն՝ ընդգրկելով 346 կին՝ 16–51 տարեկան, ովքեր հղիացել էին IVF-ի միջոցով: Մասնակիցները ներառում էին միապտուղ և բազմապտուղ հղիություններ՝ խմբավորված ըստ մոր տարիքի և պտուղների թվի: Վերահսկիչ խումբը ձևավորվել էր 1:2 հարաբերակցությամբ՝ համապատասխանեցված մոր տարիքի և ծննդաբերությունների քանակի հետ: Համեմատվել են դեմոգրաֆիկ բնութագրերը, բժշկական պատմությունը, հղիության հետ կապված բարդությունները և մայրական ու նորածնային արդյունքները: IVF հղիությունների շրջանում կանանց 12,4%-ը ≥36 տարեկան էին, 31,3%-ը՝ 30–35 տարեկան, իսկ 56,3%-ը՝ <30 տարեկան: Անպտղության հիմնական պատճառը եղել է տղամարդկանց գործոնը (59,6% դեպքերում), որին հետևում են համակցված կանանց և տղամարդկանց անպտղությունը (6,9%), ձվազատման խանգարումները (10,3%), անպատճառ անպտղությունը (4,6%) և էնդոմետրիոզը (3,5%): Ռոբսոնի դասակարգումը հայտնաբերեց, որ 6; 5,1; 4b; 9; 7; 2b և 10 խմբերն են հիմնականում նպաստում ԿՀ ցուցանիշների բարձրացմանը: IVF և վերահսկիչ խմբերի մայրական բնութագրերն ու բարդությունները համեմատելի էին:

Ռոբսոնի դասակարգումն արժեքավոր գործիք է՝ ծննդաբերության ելքերը գնահատելու և բարելավման ուղղություններ բացահայտելու համար: Չնայած IVF-ի առաջընթացին՝ ԿՀ մնում են գերակշռող, ինչը կարևորվում է ծննդաբերության մեթոդի անհատականացված ընտրությամբ՝ մայրական և նորածնային ելքերն օպտիմալացնելու համար:

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