Conception by means of in vitro fertilization is not associated with maternal depressive symptoms during pregnancy or postpartum

Pietro Gambadauro, M.D., Ph.D.,[a,b] Stavros Iliadis, M.D., Ph.D.,[b] Emma Bränn, M.Sc.,[b] and Alkistis Skalkidou, M.D., Ph.D.[b]

[a] Department of Learning, Informatics, Management and Ethics (LIME), Karolinska Institutet, Stockholm; and [b] Department of Women's and Children's Health, Uppsala University, Uppsala, Sweden

Objective: To study whether conception by means of in vitro fertilization (IVF) is associated with maternal depressive symptoms during pregnancy or postpartum.
Design: Longitudinal observational study.
Setting: University hospital.
Patient(s): A total of 3,283 women with singleton pregnancies receiving antenatal care and delivering in Uppsala from 2010 to 2015.
Intervention(s): A web-based self-administered structured questionnaire including sociodemographic, clinical and pregnancy-related items, and the Edinburgh Postnatal Depression Scale (EPDS) was delivered at 17 and 32 gestational weeks and at 6 weeks and 6 months postpartum.
Main Outcome Measure(s): Prevalence of significant depressive symptoms (EPDS ≥ 12) and EPDS scores.
Result(s): A total of 167 women (5%) had conceived via IVF and 3,116 (95%) had a spontaneous pregnancy. IVF mothers were more frequently ≥ 35 years of age (46.1% vs. 22.6%) and primiparous (71.7% vs. 49.9%) and had a higher cesarean delivery rate (22.4% vs. 14.2%). Demographic and clinical characteristics were otherwise similar between the two groups. Significant depressive symptoms were reported by 12.8%, 12.4%, 13.8%, and 11.9% of women at 17 and 32 gestational weeks and 6 weeks and 6 months postpartum, respectively. The prevalence of depressive symptoms and the EPDS scores during pregnancy and postpartum were similar between women conceiving spontaneously or through IVF. The mode of conception was not associated with significant depressive symptoms at any time point, even when adjusting for several possible confounders in multivariable logistic regression analysis.
Conclusion(s): Despite the psychologic distress characterizing subfertility and its treatment, conception by means of IVF is not associated with maternal depressive symptoms during pregnancy or postpartum. (Fertil Steril® 2017;■:■–■. ©2017 by American Society for Reproductive Medicine.)
Key Words: In vitro fertilization, assisted reproductive technologies, pregnancy complications, depression, postpartum depression

In vitro fertilization (IVF) was an acknowledged breakthrough in medical history (1, 2), and its scope has been successfully extended far beyond the initial indications due to multiple factors, including social, technical, and commercial ones (3, 4). In 2012 it was estimated that 5 million children had already been born worldwide (5), and in some countries a considerable, and increasing, share of newborns are conceived via IVF (6, 7).

Although most of the research in this field has its natural focus on the desired reproductive outcomes, namely, pregnancies and live births, the question of whether conception by IVF is associated with perinatal depression has been addressed more rarely. Yet maternal depressive symptoms, whether occurring during pregnancy or culminating in the postpartum period, are a common and major contributor to maternal morbidity and mortality (8). Furthermore, psychologic distress is, unsurprisingly, associated with subfertility (9), and several studies show a high prevalence of anxiety and

Received February 27, 2017; revised June 4, 2017; accepted June 6, 2017.
P.G. reports personal fees from Merck AB and Gedeon Richter Nordics AB; and non-financial support from Karl Storz and Ethicon. S.I. has nothing to disclose. E.B. has nothing to disclose. A.S. has nothing to disclose.
The BASIC project received grants from the Swedish Medical Association, Marianne and Marcus Wallenberg Foundation, Swedish Research Council, and Uppsala University Hospital.
Reprint requests: Pietro Gambadauro, M.D., Ph.D., Karolinska Institutet, LIME/NASP-C7, 17177 Stockholm, Sweden (E-mail: pietro.gambadauro@ki.se; gambadauro@gmail.com).

Fertility and Sterility® Vol. ■, No. ■, ■ 2017 0015-0282/$36.00

http://dx.doi.org/10.1016/j.fertnstert.2017.06.006

depression among couples undergoing IVF (9–11). Treatment failures are particularly linked to psychologic distress (12), but even successful IVF mothers may experience a complex transition to parenthood with intense fetal attachment and anxiety (13–15). Nevertheless, relatively few well controlled studies with heterogeneous design have focused on the association between successful IVF and maternal depression. Some authors have documented a positive association between depressive perinatal maternal symptoms and conception by IVF (16), and related factors, such as multiple pregnancies, have been suggested to increase the risk (17). However, a recent meta-analysis of observational studies rejected the hypothesis that pregnancies conceived through medically assisted conception or assisted reproductive technologies (ART) are associated with postpartum depressive symptoms (18). Unfortunately, only six studies specifically focusing on ART were available for inclusion in analysis (16, 19–23), four of them originating from Australia (19, 20, 22, 23), accounting for a total of 1,773 women (18). A further obstacle to the synthetic interpretation of the few available studies is a substantial heterogeneity in case selection, design, and outcome measurements. Many include women conceiving with the use of ART treatments other than IVF (e.g., gamete intrafallopian transfer), or through gamete donation. The outcome variables also differ across published studies and have not always been measured by validated instruments. The internationally validated Edinburgh Postnatal Depression Scale (EPDS) (24) was sometimes used, albeit at different or unspecified time points. A study reported significantly higher EPDS scores among ART mothers at 30–32 gestational weeks and at 1 week and 3 months postpartum (16). The same authors found more depressed subjects, defined by EPDS >12, among the ART mothers during the 3rd trimester (16% vs. 0%) as well as at 1 week (12% vs. 7.9%) and 3 months (8% vs. 0%) postpartum, although only the antenatal difference was statistically significant (16). No significant differences in prevalence of depressive symptoms (EPDS ≥13) between ART (5%) and non-ART (7%) mothers were reported by another study at 12 months postpartum (19). Clinically relevant depressive symptoms (EPDS >12) among patients of a mother-baby unit, who presented with infant sleeping/feeding problems or maternal psychologic distress during the 1st year postpartum, were unsurprisingly frequent (>45% of women) regardless of the mode of conception (ART or spontaneous) (20). However, ART mothers were significantly overrepresented in that selected group of women (6% vs. 1.52% in the general population), and the mode of conception was not recorded for 219 cases (29.4%), which were included as spontaneous (20). McMahon et al. (22) observed no differences at 4 months postpartum between IVF and spontaneous mothers in the rate of major depressive disorder as diagnosed by a structured interview (Mini-Plus International Neuropsychiatric Interview). However, the prevalence of major depression was higher among IVF mothers in the age stratum of ≥31 to <37 years (11.6% vs. 3.6% in spontaneous pregnancies) (22), which is a well represented age group among ART patients. Through telephone interviews conducted up to 2 years after delivery, no significant differences between ART and spontaneous mothers were found when asking "whether they believed that they had postnatal depression" during the first 4 weeks (23).

Registry studies including large populations also have failed to show an association between fertility treatments and postpartum depression (25, 26). However, they may be limited by a cross-sectional design, the inability to differentiate between different kinds of fertility treatments (25), or the need to rely retrospectively on registered treatments and coded diagnoses of depression (26).

Finally, most studies on postpartum depression, as well as the only available meta-analysis (18), neglect antenatal symptoms, although these are known as a significant risk factor (27) if not an earlier manifestation of the same condition (8). Findings from studies specifically addressing antenatal depressive symptoms among IVF mothers have so far been contrasting, including similar, higher, or even lower rates compared with spontaneously pregnant women (16, 28–30).

Clearly, the question of whether exposure to IVF conception alone is associated with perinatal depression has not been explored thoroughly. Therefore, our current view on this relevant and complex topic is neither as broad nor as deep as it should be, particularly in a context of evolving and cross-nationally heterogeneous IVF practices. Ideally, larger prospective studies, measuring depressive symptoms with the use of validated instruments both during pregnancy and postpartum and focusing on IVF patients while removing or controlling for potential confounders or effect modulators, would be needed. Furthermore, prospective data from so far underrepresented geographic regions as well as from modern single embryo transfer (SET) contexts would be desirable. The aim of the present study was to evaluate whether conception by IVF is associated with maternal depressive symptoms, both during pregnancy and postpartum, in a large prospective cohort of pregnant women receiving obstetrical care at a Swedish university hospital.

MATERIALS AND METHODS

Study Population

This study was conducted at the Department of Obstetrics and Gynecology of Uppsala University Hospital, Uppsala, Sweden, as a part of the BASIC (Biology, Affect, Stress, Imaging, Cognition) project, a population-based longitudinal study on psychologic well-being during pregnancy and postpartum (31). From 2010 to 2015, pregnant women undergoing routine fetal ultrasound screening at gestational week 17 were informed about the project and asked to give their consent to participate. Exclusion criteria at this stage included: age <18 years, protected identity, inability to adequately communicate in Swedish, and pathologic findings at the routine ultrasound scan. Participation was not compensated, and the original BASIC cohort had a participation rate of 22%. Participants were asked to complete a web-based self-administered structured questionnaire containing questions on sociodemographic, clinical and pregnancy-related variables, and a Swedish validated version of the EPDS (24, 31), at 17 and 32 gestational weeks and 6 weeks and 6 months