DOI: 10.1111/1471-0528.13910
www.bjog.org

Systematic Review

Donor oocyte conception and pregnancy complications: a systematic review and meta-analysis

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Accepted 11 December 2015. Published Online 8 February 2016.

Background Observational studies showed that women with a donor oocyte (DO) pregnancy have an increased risk of pregnancy complications.

Objectives Systematic review and meta-analysis to compare pregnancy complications of DO pregnancy with autologous oocyte *in vitro* fertilisation (IVF), and whether DO pregnancy acts as an independent risk factor.

Search strategy Online searches of databases from 1 January 1980 to 31 January 2015 were performed using a set of relevant keywords.

Selection criteria All studies comparing pregnancy complications of women with donor oocyte IVF and autologous oocyte IVF were included.

Data collection and analysis Data collected included demographics and pregnancy complications. Methodological quality assessment was performed using the Newcastle–Ottawa scale. Statistical analysis was performed using REVIEW MANAGER 5.3 and STATA 13.0. Meta-regression was performed for age.

Main results In total, 11 studies (n = 81 752) were included. Ten studies (n = 11 539) examined the primary outcome. The risk of developing hypertensive disorders in pregnancy was significantly higher for DO pregnancy (odds ratio, OR 3.92; 95% confidence interval, 95% CI 3.21–4.78). Further subgroup analysis for singleton and twin pregnancies showed that the risk was significantly higher for DO pregnancy in each group. Secondary outcomes including small for gestational age (OR 1.81), caesarean section (OR 2.71), and preterm delivery (OR 1.34) were significantly higher with DO pregnancy. Meta-regression for the covariate of age suggested that risk was independent of age.

Author's conclusions Donor oocyte pregnancy acts as an independent risk factor for pregnancy complications, including hypertensive disorders, small for gestational age, and preterm delivery. Women should be counselled carefully before undergoing DO-assisted conception.

Keywords Donor oocyte pregnancy, *in vitro* fertilisation, pre-elampsia, pregnancy-induced hypertension.

Tweetable abstract Donor oocyte conception is an independent risk factor for obstetric complications.

Please cite this paper as: Jeve YB, Potdar N, Opoku A, Khare M. Donor oocyte conception and pregnancy complications: a systematic review and meta-analysis. BJOG 2016; DOI: 10.1111/1471-0528.13910.

Introduction

Donor oocyte (DO) conception has allowed many women of advanced age to achieve successful pregnancies. The demand has grown steadily with the trend of delayed child-bearing. This phenomenon of increased maternal age is likely to continue in the years to come.[1] The recent rise in DO pregnancies is reported by all European countries.[2] In addition to advanced maternal age there are various other indications for DO conception, which include primary or secondary ovarian failure, diminished ovarian reserve, multiple failures of *in vitro* fertilisation (IVF), and diagnoses of genetic conditions.[3] The treatment option of egg sharing, which involves a woman sharing her eggs with another in exchange for free or reduced-cost fertility treatment, has been regulated in the UK since 1998, and is viewed positively by the egg-sharing donors and recipients.[4] Advanced maternal age in itself is associated with pregnancy complications, including hypertensive disorders, gestational diabetes, preterm labour, and intrauterine growth

restriction.[5,6] A recent report from the Human Fertilization and Embryonic Authority (HFEA) showed that over half of women receiving IVF aged 45 years and older used donated oocytes, but that there has also been a substantial increase in recipients aged under 35 years.[7] The most common complication noted in DO pregnancies is pregnancy-induced hypertension and pre-eclampsia, ranging from 16 to 40% of women.[8–13] Pre-eclampsia affects 3–5% of all pregnancies, and is estimated to result in 60 000 maternal deaths annually worldwide.[14] Although obstetric complications have been attributed to advanced maternal age in these women, the risk is reported to be independent of age.[13] Placental pathology as a result of immunological pathogenesis is suggested to be the reason for obstetric complications in DO pregnancy. The study by Kim et al.[15] showed that the incidence of hypertensive disorders is significantly higher if the oocyte donor is unrelated to the recipient, compared with a related sibling donor. It is suggested that immunologic intolerance between the mother and the fetus may play an important role in the pathogenesis of pre-eclampsia.[16–18] Pregnancies achieved by IVF or by intracytoplasmic sperm injection (ICSI) are at a higher risk for pregnancy complications compared with spontaneous pregnancies.[19] Therefore, it would be more appropriate to use autologous-oocyte IVF pregnancy as a control group to study outcome in DO pregnancies.

The aim of this systematic review and meta-analysis is to study the obstetric outcome of DO pregnancies compared with autologous-oocyte IVF pregnancy. We aim to discover whether DO pregnancy acts as an independent risk factor for pregnancy complications.

Methods

A literature search was performed using Ovid MEDLINE® (1980–January 2015), EMBASE (1980–January 2015), Ovid OLDMEDLINE®, Pre-MEDLINE, in-process and other non-indexed citations database consists of in-process and PubMed-not-MEDLINE records from NLM, HaPI (1985–January 2015), Google scholar, Web of Sciences (1980–2015), and the Cochrane Library. The conference proceedings citation index was also searched with no language restriction applied. A combination of medical subject headings and keywords were used to generate a subset of: citations for oocyte* ('ovum', 'ova', 'egg*'); citations including donor and oocyte; citations including assisted conception techniques ('ART* or IVF* or ICSI*'); and citations including various pregnancy complications ('gestational hypertension or pregnancy-induced hypertension or pre-eclampsia*' 'fetal growth restriction* or IUGR* or small baby or birthweight', 'preterm labour', 'intrauterine death*', 'caesarean section*'). These subsets were combined using 'AND' or 'OR', as appropriate, to generate a set of results addressing the research question. Duplicates were removed. The reference list of all published articles including review articles was examined to check for missed citations. No author was contacted. This review was registered in the PROSPERO database (CRD42015023739).

Data collection and analysis

Two review authors (YJ and NP) independently screened the titles and abstracts. Studies that met the predefined and explicit criteria were selected for inclusion in the review. The electronic searches were scrutinised and the full texts of all citations that were likely to meet the predefined selection criteria were obtained. The quality of included citations was independently examined and data extraction was performed. Where disagreements occurred, they were resolved by the consensus of both authors.

Criteria for including studies in the review

Types of study

Inclusion criteria: all observational studies comparing pregnancy outcomes in DO pregnancies with a predefined control group of pregnancies achieved with autologous oocyte IVF or ICSI only. Studies comparing outcome of DO singleton and twin gestations were included. All published data were used in the review. We have included both prospective and retrospective cohort and case–control studies.

Exclusion criteria: all observational studies reporting outcome in only DO pregnancies without any control group were excluded. Studies with incomplete data or with a heterogeneous control group were excluded. All studies with a spontaneous conception group used as the control group, donor sperm conception, case reports, and DO conception for Turner syndrome were also excluded, as Turner syndrome itself carries an additional risk for obstetric complications.

Types of participants

Women who conceived as a result of DO-assisted conception and delivered at 24 weeks of gestation, or later, were included in the analysis. The control group included women who had assisted conception using IVF or ICSI with autologous oocytes.

Types of outcome measures

The primary outcome was any hypertensive disorder in pregnancy, which included pregnancy-induced hypertension (PIH) and pre-eclampsia (PET). PIH was defined as a blood pressure of ≥140/90 mmHg on two or more occasions, at least 6 hours apart, without proteinuria, and later than 20 weeks of gestation. PET was defined as a blood

pressure of ≥140/90 mmHg on two or more occasions, at least 6 hours apart, with proteinuria of ≥0.3 g/day, and later than 20 weeks of gestation. This definition was consistent with the definition set by the International Society for the Study of Hypertension in Pregnancy (ISSHP).[20] Subgroup analysis was performed for PIH and PET separately in singleton DO pregnancies.

Secondary outcome measures included risk of caesarean section, development of gestational diabetes, small for gestational age, preterm delivery, and intrauterine death (IUD). Small for gestational age (SGA) was defined as a birthweight of less than tenth centile. For the purpose of standardisation, we have used the term SGA. The terms fetal growth restriction (FGR) or intrauterine growth restriction (IUGR) have been used by some authors, although all of these fulfil the criteria for SGA based on birthweight. Preterm labour was defined as delivery before 37 completed weeks of gestation.

Quality and risk of bias of the included studies

All studies included were cohort and case–control studies. Quality assessment was performed using the internationally accepted Newcastle–Ottawa scale.[21] The Newcastle–Ottawa scale evaluates the quality of non-randomised studies, and focuses on the design, content, and ease of use for incorporating the quality of assessments in the interpretation of meta-analytic results. This scale is useful to evaluate potential biases at selection, comparability, exposure, and outcome stages. The selected studies were assessed for methodological quality using the domain-based risk for bias assessment tool, as recommended by the Cochrane Collaboration.[22] A risk-of-bias table was produced in REVMAN 5.3,[23] using the biases described by the Newcastle–Ottawa scale.

Statistical analysis

The study characteristics and outcomes were assembled in tabular form. A formal meta-analysis was performed using REVMAN 5.3.[23] A fixed-effect model (using the Mantel–Haenszel method) was used when the I^2 statistic showed heterogeneity of <50%, whereas a random-effect model was used when the I^2 statistic showed heterogeneity >50%. The effect estimate was expressed as an odds ratio (OR) with a 95% confidence interval (95% CI), represented graphically by forest plots. Clinical heterogeneity was examined by assessing the participants, intervention used, study quality, and outcome measures. Statistical heterogeneity was examined using the χ^2 test, with $P < 0.05$ taken as suggestive of heterogeneity. Publication bias was assessed visually using a funnel plot and by formal testing. Meta-regression was performed using STATA 13.0 to determine whether age at conception was a limiting factor between studies (Figure S1).

Results

The process of literature search and study selection for the quantitative meta-analysis is shown in Figure 1. We reviewed 43 full-text articles after the screening search and excluded 32 articles, with the most common reason for exclusion being inappropriate control group. A total of 11 studies including 81 752 cycles were included in the review and meta-analysis. The characteristics of the included studies are shown in Table S1.

Meta-analysis

Primary outcome

The primary outcome measure was hypertensive disorders of pregnancy, which included PIH and PET. We found that the risk of developing hypertensive disorders in pregnancy was significantly higher in the DO pregnancy group than in autologous oocyte IVF pregnancy. The fixed-effect model for ten studies showed women with DO pregnancy ($N = 970$) had a significant risk of developing hypertensive disorders in pregnancy [$n/N = 341/970$ (35%) in the DO group versus $n/N = 1831/10569$ (17%) in the autologous IVF group; OR 3.92, 95% CI 3.21–4.78, $I^2 = 10\%$; Figure 2]. We performed subgroup analysis for four studies with twin pregnancies,[13,24–26] and the fixed-effect model showed that hypertensive disorders of pregnancy were significantly higher in DO twin pregnancy than in the autologous twin pregnancy group [$n/N = 89/229$ (38%) versus $n/N = 948/5630$ (16%), OR 3.69, 95% CI 2.62–5.19, $I^2 = 0\%$; Figure 2]. The subgroup analysis for PET in singleton DO pregnancies included four studies,[18,24,27,28] and the fixed-effect model showed that the risk of PET was significantly higher in singleton DO pregnancy [$n/N = 66/606$ (10%) versus $n/N = 333/10193$ (3%), OR 2.90, 95% CI 1.98–4.24, $I^2 = 0\%$; Figure 3]. The fixed-effect model meta-analysis of five studies showed that the risk of PIH in singleton DO pregnancy is significantly higher when compared with singleton IVF pregnancy [$n/N = 99/577$ (17%) versus $n/N = 522/10211$ (5%), OR 3.08, 95% CI 2.26–4.19, $I^2 = 0\%$; Figure 3].[11,24,26,28,29] Additionally, the subgroup analysis fixed-effect model of two studies of women older than 40 years of age showed that the risk for hypertensive disorders was still significantly higher with DO pregnancy compared with IVF pregnancy [$n/N = 30/129$ (23%) versus $n/N = 18/168$ (10%), OR 2.33, 95% CI 1.21–4.49, $I^2 = 2\%$; Figure 3].[29,30] Meta-regression for the covariate of age showed that between-study variance was minimal ($\tau^2 = 0.008$), and that the occurrence of hypertensive disorders in the studies was independent of age, with P

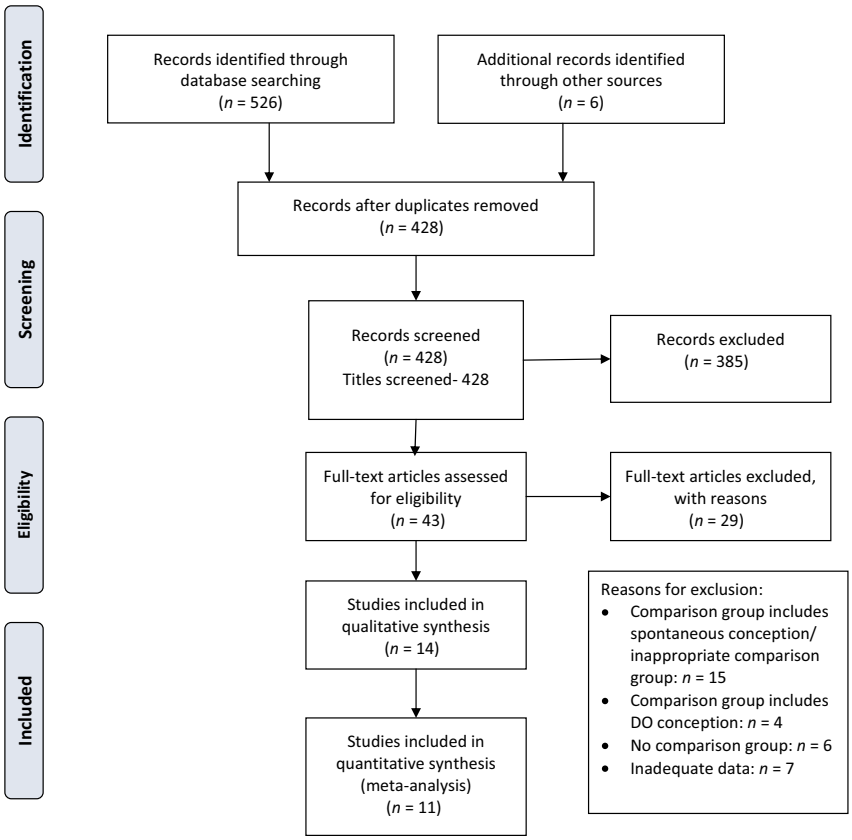


Figure 1. PRISMA 2009 flow diagram.

values above the level of significance ($P = 0.473$, 95% CI 0.90–1.05).

As both cohort and case–control studies were included in the meta-analysis, to assess the robustness of the results we performed sensitivity analysis after the exclusion of the case–control studies. Six cohort studies were included in the meta-analysis for the primary outcome measure of hypertensive disorders of pregnancy (Figure S2).[18,24,25,30–32] The analysis showed that the risk of hypertensive disorders was significantly raised in all DO pregnancies (OR 3.63, 95% CI 2.92–4.51, $I^2 = 0\%$). This effect was significant for singleton (OR 3.05, 95% CI 2.19–4.24, $I^2 = 0\%$) as well as twin pregnancies (OR 3.64, 95% CI 2.57–5.16, $I^2 = 0\%$). Risk for PET in the singleton DO subgroup also showed a significant difference (OR 2.62, 95% CI 1.75–3.93 $I^2 = 0\%$).

Secondary outcome

Secondary outcome measures included SGA, preterm delivery, risk of caesarean section, gestational diabetes, and intrauterine death (IUD). Meta-analysis of six studies showed that the risk of SGA was significantly raised in DO pregnancy [$n/N = 58/630$ (9%) versus $n/N = 594/11262$ (5%), OR 1.81, 95% CI 1.26–2.60, $I^2 = 21\%$].[11,18,24,27,31,32] As a result of uncertainty about the definition used to define SGA in the original papers, however, subgroup analysis was performed for three studies with consistent definition, and the results gave OR 1.44 [$n/N = 34/422$ versus $n/N = 585/11\,044$, OR 1.44, 95% CI 0.93–2.23, $I^2 = 0\%$].[11,18,24] Because of the discrepancy in the definitions used for identifying FGR, IUGR, and SGA, these results should be interpreted with caution. Birthweight reported in six studies showed no significant difference (Figure 4).[11,24,29,32–34] The risk of preterm delivery was analysed in nine studies, and the fixed-effect model showed that the risk of preterm birth was significantly higher in DO pregnancy compared with autologous IVF pregnancy [$n/N = 194/1011$ (19%) versus $n/N = 1078/11\,651$ (9%), OR 1.34, 95% CI 1.08–1.66, $I^2 = 38\%$; Figure 4].[18,24,26,29–32,35–37] The risk of caesarean section was significantly increased in DO pregnancy [$n/N = 435/690$ (88%) versus $n/N = 3452/10\,283$ (33%), OR 2.71, 95% CI 2.23–3.30, $I^2 = 43\%$; Figure 4].[11,18,24,26,37,38] Neither the increased risk of IUD, analysed in two studies [$n/N = 4/303$ (1.3%) versus $n/N = 3/346$ (0.8%), OR 1.39, 95% CI 0.32–6.15],[35,37] nor the increased risk of developing gestational diabetes for the mother, analysed in five studies [$n/N = 58/524$ (11%) versus $n/N = 52/519$ (10%),

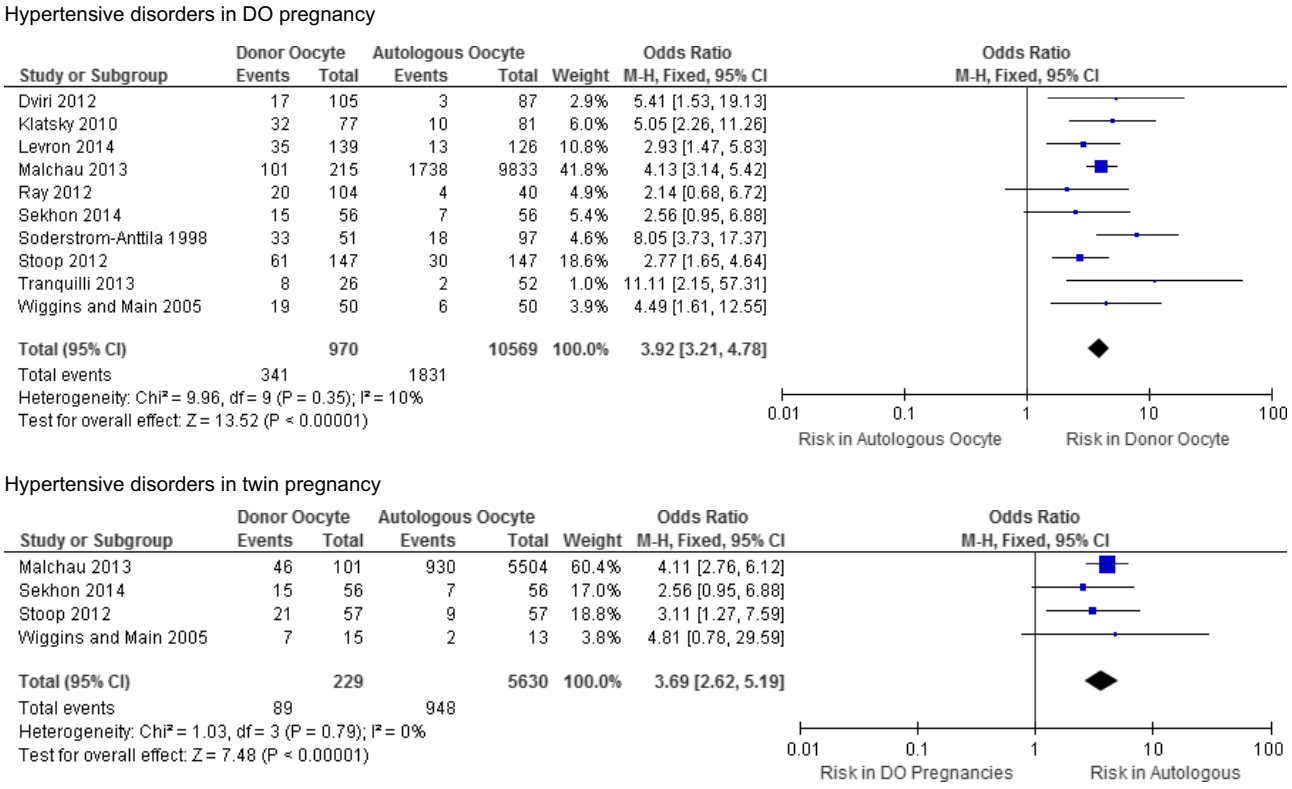


Figure 2. Primary outcome- Hypertensive disorders in DO pregnancy.

OR 1.25, 95% CI 0.68–2.30],[11,18,26,32,37] was statistically significant.

Discussion

Main findings

The results of the meta-analysis described above show that the risk of developing hypertensive disorders in pregnancy is significantly higher with DO pregnancy when compared with autologous IVF pregnancy. The studies included singletons as well as twins; therefore, we studied the effect in singleton and multiple pregnancies separately. The increased risk was found in all subgroups, including women of advanced maternal age. When the risk of hypertensive disorders in pregnancy was subdivided into two groups, PIH and PET, the risk of both complications was higher in DO pregnancies. These findings are consistent with some previous observational studies.[8–12,29,30] Multiple pregnancy is a known risk factor for developing hypertensive disorders; however, our analysis suggested that DO pregnancy is independent of multiple pregnancies for the development of hypertensive disorders. The risks of SGA and preterm delivery are significantly higher in DO pregnancy. Our meta-analysis showed that the chances of caesarean delivery for singletons are significantly higher with DO pregnancy. Similar findings are reported by other authors.[3,9,10,12]

Strengths and limitations

This is the first meta-analysis and meta-regression to quantify the risk of pregnancy complications in women with DO pregnancy. A previous systematic review by van der Hoorn focused on the immunological pathogenesis of complications, but did not include meta-analysis.[39] We have quantified the risk taking into account potential confounding factors; therefore, this meta-analysis provides evidence-based information for the clinical care of women with DO pregnancy. The outcomes of DO IVF pregnancies have been compared with autologous oocyte IVF pregnancies in various subgroups, adjusting for maternal age, multiple gestation, and the assisted reproductive technique. The meta-analysis showed small values for I^2 and narrow confidence intervals. This suggests that the accuracy of the meta-analysis is of good quality, and that the estimated value is relatively stable. Low statistical heterogeneity is a major strength of our meta-analysis. A previous systematic review and meta-analysis performed by Pecks showed that DO is a risk factor for the development of PIH; however, the control group included all types of conventional reproductive therapy, including spontaneous conception.[40] Shanis showed that IVF itself increases the risk of PET.[41] The systematic review by van-der Hoorn concluded that the higher risk of maternal morbidity in DO pregnancy is

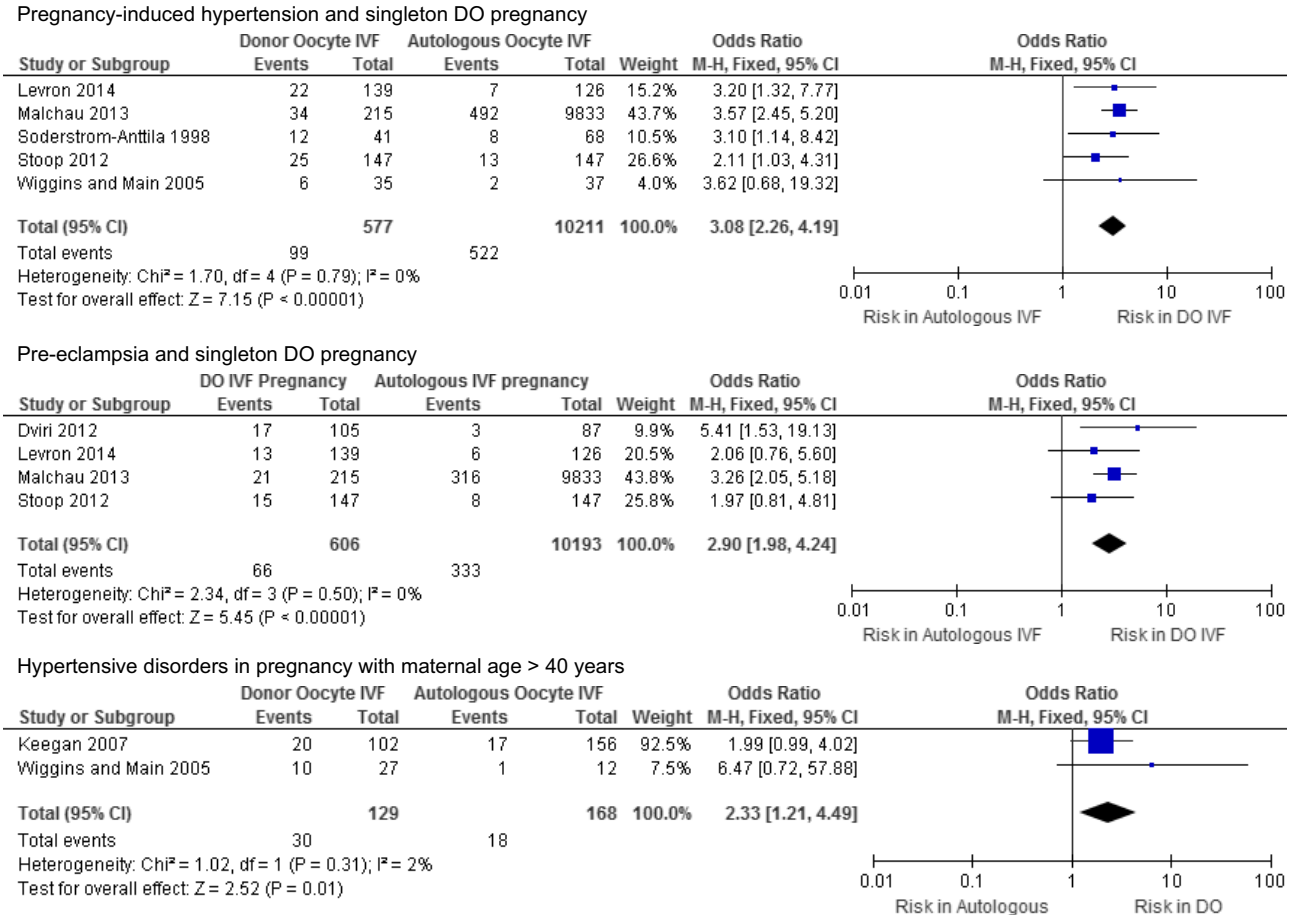


Figure 3. Primary outcome – subgroup analysis.

linked to the high degree of antigenic dissimilarity.[17] In original publications the definitions of FGR, IUGR, or SGA are not standardised. These definitions have evolved over a period of time. We have performed sensitivity analysis to address this limitation. We have used the term SGA, which covers all babies with birthweights of less than the tenth centile. Although we made every attempt to neutralise the effects of confounding factors such as age by performing subgroup analysis and meta-regression, it is difficult to prove that the risk is totally independent of these variables from any meta-analysis and systematic review. It requires a multivariate analysis on an original data set. Ideally, individual participant data (IPD) meta-analysis would be the best design to assess the effect of various other confounding factors. The secondary outcomes of preterm delivery, SGA, and caesarean section may be the result of hypertensive disorders in pregnancy. It is not possible to identify the magnitude of these complications independent of hypertensive disorders. Analysis of any complication as an outcome depends upon prevention and management strategies. The information was not available on preventative measures such as the use of low-dose aspirin or ultrasound assessment for fetal growth.

Interpretation

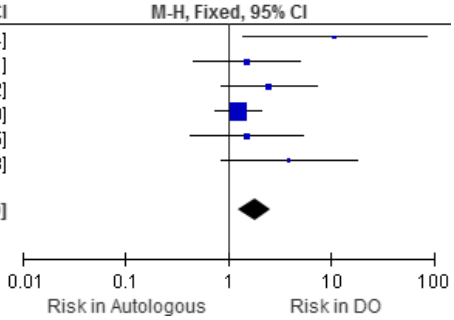
Donor oocyte (DO) IVF provides the opportunity of pregnancy for many women, but at the same time increases the risks associated with pregnancy. Multiple gestations, advanced age, and underlying polycystic ovary syndrome are constant confounding factors for all studies examining the association between assisted reproductive techniques (ARTs) and hypertensive disorders in pregnancy.[42] Thomopoulos showed that ART pregnancies, especially IVF techniques, are accompanied by increased risks for gestational hypertension and PET, as compared with non-ART pregnancies, even after adjustment for confounding factors.[42]

The success of pregnancy depends upon an appropriate implantation and placental function. Any insult during the process of implantation and placentation leads to obstetric complications, including spontaneous miscarriage, SGA, preterm birth, and PET.[43] The risk of hypertensive disor-

Small for Gestational Age and DO pregnancy

Study or Subgroup	DO Pregnancy Events	DO Pregnancy Total	Autologous Oocyte Events	Autologous Oocyte Total	Weight	Odds Ratio M-H, Fixed, 95% CI
Dviri 2012	12	105	1	85	2.5%	10.84 [1.38, 85.14]
Klatsky 2010	7	77	5	81	11.3%	1.52 [0.46, 5.01]
Levron 2014	13	139	5	126	12.1%	2.50 [0.86, 7.22]
Malchau 2013	16	244	574	10850	60.2%	1.26 [0.75, 2.10]
Soderstrom-Anttila 1998	5	39	6	68	9.7%	1.52 [0.43, 5.35]
Tranquilli 2013	5	26	3	52	4.1%	3.89 [0.85, 17.78]
Total (95% CI)		**630**		**11262**	**100.0%**	**1.81 [1.26, 2.60]**
Total events	58		594			

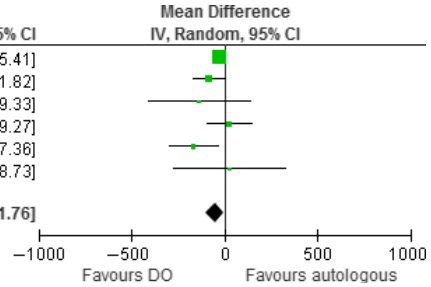
Heterogeneity: Chi² = 6.32, df = 5 (P = 0.28); I² = 21%
Test for overall effect: Z = 3.22 (P = 0.001)



Birth weight and DO pregnancy

Study or Subgroup	DO Pregnancy Mean	DO Pregnancy SD	DO Pregnancy Total	Autologous Oocyte Mean	Autologous Oocyte SD	Autologous Oocyte Total	Weight	Mean Difference IV, Random, 95% CI
Gibbons 2011	3,236	652.7	10176	3,265	611	60037	51.8%	−29.00 [−42.59, −15.41]
Malchau 2013	3,298	677	244	3,382	649	10850	19.9%	−84.00 [−169.82, 1.82]
Soderstrom-Anttila 1998	3,338	740	39	3,475	630	68	2.9%	−137.00 [−413.33, 139.33]
Stoop 2012	2,832.9	709.9	262	2,805.3	711.1	262	12.1%	27.60 [−94.07, 149.27]
Tranquilli 2013	2,925	330	26	3,093	115	52	10.9%	−168.00 [−298.64, −37.36]
Wiggins and Main 2005	3,044	751	50	3,017	788	50	2.4%	27.00 [−274.73, 328.73]
Total (95% CI)			**10797**			**71319**	**100.0%**	**−49.89 [−98.03, −1.76]**

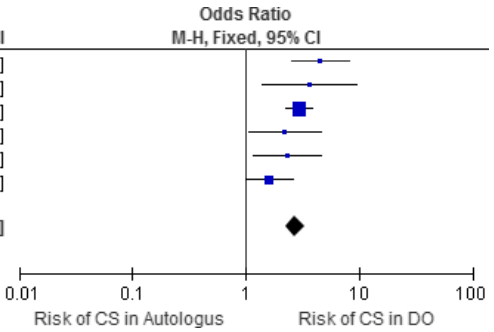
Heterogeneity: Tau² = 1115.85; Chi² = 7.37, df = 5 (P = 0.19); I² = 32%
Test for overall effect: Z = 2.03 (P = 0.04)



Caesarean section and DO pregnancy

Study or Subgroup	DO Pregnancy Events	DO Pregnancy Total	Autologous oocyte Events	Autologous oocyte Total	Weight	Odds Ratio M-H, Fixed, 95% CI
Levron 2014	118	139	70	126	9.3%	4.50 [2.51, 8.05]
Lin 2011	27	36	19	42	3.7%	3.63 [1.38, 9.57]
Malchau 2013	128	215	3258	9833	47.3%	2.97 [2.25, 3.91]
Ray 2012	62	104	16	40	7.8%	2.21 [1.05, 4.66]
Soderstrom-Anttila 1998	29	51	35	97	8.7%	2.34 [1.17, 4.66]
Stoop 2012	71	145	54	145	23.1%	1.62 [1.01, 2.58]
Total (95% CI)		**690**		**10283**	**100.0%**	**2.71 [2.23, 3.30]**
Total events	435		3452			

Heterogeneity: Chi² = 8.81, df = 5 (P = 0.12); I² = 43%
Test for overall effect: Z = 9.94 (P < 0.00001)



Preterm delivery and DO pregnancy

Study or Subgroup	DO Pregnancy Events	DO Pregnancy Total	Autologous Oocyte Events	Autologous Oocyte Total	Weight	Odds Ratio M-H, Fixed, 95% CI
Bellver 2007	32	131	38	206	16.0%	1.43 [0.84, 2.43]
Klatsky 2010	26	77	15	81	6.9%	2.24 [1.08, 4.67]
Levron 2014	12	139	12	126	8.2%	0.90 [0.39, 2.08]
Lin 2011	6	36	4	42	2.2%	1.90 [0.49, 7.35]
Malchau 2013	35	244	930	10850	25.1%	1.79 [1.24, 2.57]
Ray 2012	30	104	10	40	7.3%	1.22 [0.53, 2.79]
Stoop 2012	32	204	44	204	26.5%	0.68 [0.41, 1.12]
Tranquilli 2013	13	26	20	52	4.8%	1.60 [0.62, 4.14]
Wiggins and Main 2005	8	50	5	50	3.0%	1.71 [0.52, 5.66]
Total (95% CI)		**1011**		**11651**	**100.0%**	**1.34 [1.08, 1.66]**
Total events	194		1078			

Heterogeneity: Chi² = 12.89, df = 8 (P = 0.12); I² = 38%
Test for overall effect: Z = 2.69 (P = 0.007)

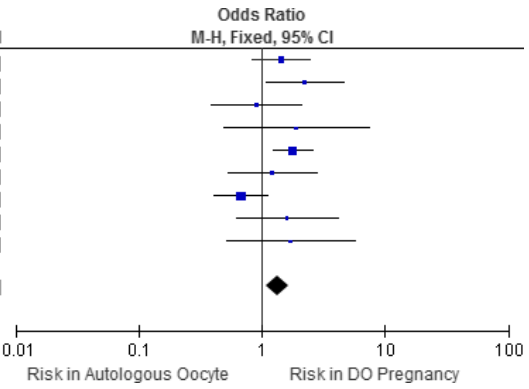


Figure 4. Secondary outcomes.

ders of pregnancy in DO pregnancies can be explained on the basis of an immunological mechanism.[44,45] In DO pregnancies the fetus is allogeneic to the gestational carrier. Therefore, the mother has to cope with a higher degree of antigenic dissimilarity compared with spontaneously conceived pregnancies.[46,47] Increased immunological activity and fibrinoid deposition was noted at the maternal–fetal interface in DO pregnancies.

This represents a host versus graft rejection-like phenomenon.[48] Parental human leukocyte antigen sharing plays a role in the aetiology of PET.[49] Considering the immunologic mechanisms at work in DO, it might be worthwhile performing human leukocyte antigen (HLA) typing of the donor and the recipient in order to select haplo-identical combinations that would be more comparable with spontaneously conceived pregnancies than fully HLA mismatched combinations.[39] This makes DO pregnancies at higher risk of perinatal complications. Further research is required to explain the pathogenesis of DO pregnancies and placental complications.

Although the DO technique proved to be an excellent treatment option for many women to achieve pregnancy, it exposes them to higher risks of many maternal complications, including maternal death.[50–52] Women undergoing DO conception should be counselled before conception about the increased risks during DO pregnancy, and that the risk is independent of age or multiple pregnancies.[51,52] Obstetricians should be aware of the increased pregnancy risks in this particular group of patients, and appropriate surveillance strategies should be in place during antenatal, intrapartum, and postnatal care.[51] The use of serial growth scans to diagnose SGA has resource implications. Therefore, an individualised surveillance and management strategy should be considered. The use of low-dose aspirin in DO pregnancy in the absence of any other risk factors requires further evaluation. Oocyte cryopreservation for future fertility is suggested as an alternative for avoiding DO in selected cases;[34] however, data on success rates, the effect on continuing pregnancy, and adverse effects are limited.[53]

Conclusion

In the light of current evidence, DO pregnancy should be considered as an independent risk factor for pregnancy complications, including hypertensive disorders of pregnancy, SGA, preterm delivery, and caesarean section. Women should be counselled carefully about these risks before undergoing DO-assisted conception. These women should be managed in high-risk obstetric clinics with individualised monitoring and management strategies to reduce complications. The role of low-dose aspirin in DO pregnancy in the absence of any other risk factors requires further research. The use of serial growth scans in DO pregnancies needs further evaluation. Limited evidence attributed these complications to immunological origin; further research is required to explain the pathogenesis involved in donor oocyte pregnancies.

Disclosure of interests

None declared. Completed disclosure of interests form available to view online as supporting information.

Contribution to authorship

YJ preformed the literature search, reviews, data extraction, meta-analysis, and prepared the manuscript. NP reviewed papers as a second reviewer, performed data extraction, data analysis, and meta-regression. NP contributed to the study design and to writing the article. AO helped with data extraction and the literature search. MK contributed to the design of the study, overall quality assessment, and preparation of the final article.

Details of ethics approval

Not required.

Funding

None.

Supporting Information

Additional Supporting Information may be found in the online version of this article:

Figure S1. Risk of bias.

Figure S2. Sensitivity analysis for cohort studies.

Table S1. Study characteristics. ■

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