

#### INTRODUCTION

- Multifetal pregnancies are associated with an increased risk of maternal and perinatal morbidity and mortality compared to singleton pregnancies.
- Multifetal pregnancy reduction (MFPR) can be considered to reduce the total number of fetuses by one or more.

### OBJECTIVE

• To systematically review the literature on hypertensive disorders of pregnancy (HDP) after MFPR.

### METHODS

- A comprehensive search in PubMed, Embase, Web of Science and Scopus was performed.
- Prospective or retrospective studies reporting on MFPR from triplet or higherorder to twin compared to ongoing (i.e. non-reduced) triplets and/or twins were included.
- A meta-analysis of the primary outcome HDP was carried out using a randomeffects model.
- Subgroup analyses of gestational hypertension (GH) and preeclampsia (PE) were performed.
- Risk of bias was assessed using the Newcastle-Ottawa Quality Assessment Scale.

Amsterdam Reproduction & Development

# Hypertensive disorders of pregnancy after multifetal pregnancy reduction: a systematic review and meta-analysis

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Accepted for publication in Hypertension in Pregnancy

## **Highlights**:

MFPR in women with triplet and higher-order multifetal pregnancies decreases the risk of HDP. Twelve women should undergo MFPR to prevent one case of HDP.

Figure 1. HDP after MFPR in triplets and higher-order to twin pregnancy versus ongoing triplet pregancies

	MFPR higher-order	o twin	Ongoing	triplet		Odds Ratio	Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl	M-H, Random, 95% Cl
1.1.1 3->2							
Boulot 1993	6	28	8	45	7.2%	1.26 [0.39, 4.12]	
Herlihy 2017	5	42	7	43	6.7%	0.69 [0.20, 2.39]	
Kadhel 1998	2	17	2	24	2.9%	1.47 [0.19, 11.59]	
Lee 2022	17	327	30	225	15.2%	0.36 [0.19, 0.66]	<b>_</b>
Lipitz 1994	2	31	11	84	4.6%	0.46 [0.10, 2.19]	
Liu 2022	11	141	10	41	9.8%	0.26 [0.10, 0.67]	
Macones 1993	5	47	2	14	3.8%	0.71 [0.12, 4.16]	
Okyay 2014	1	43	9	65	2.8%	0.15 [0.02, 1.22]	
Porreco 1991	1	13	4	11	2.2%	0.15 [0.01, 1.58]	
Raval 2015	9	30	28	102	10.4%	1.13 [0.46, 2.77]	
Sivan 2002	9	85	14	103	10.5%	0.75 [0.31, 1.84]	
Subtotal (95% CI)		804		757	76.1%	0.55 [0.37, 0.83]	$\bullet$
Total events	68		125				
Heterogeneity: Tau <sup>2</sup> =	0.10; Chi <sup>2</sup> = 12.94, df =	10 (P = 0	).23); l <sup>2</sup> = 23	3%			
Test for overall effect:	Z = 2.85 (P = 0.004)						
440.0.0							
1.1.2 ≥3->2	_		_				
Angel 1999	5	16	7	23	5.7%	1.04 [0.26, 4.13]	
Razaz 2017	6	45	5	40	6.4%	1.08 [0.30, 3.84]	
Smith-Levitin 1996	14	59	30	54	11.8%	0.25 [0.11, 0.56]	
Subtotal (95% CI)		120		117	23.9%	0.58 [0.20, 1.70]	
Total events	25		42				
	0.55; Chi <sup>2</sup> = 5.29, df = 2	! (P = 0.0	7); l² = 62%	•			
Test for overall effect:	Z = 0.99 (P = 0.32)						
Total (95% CI)		924		874	100.0%	0.55 [0.38, 0.79]	•
Total events	93		167				
Heterogeneity: Tau <sup>2</sup> = 0.14; Chi <sup>2</sup> = 18.42, df = 13 (P = 0.14); l <sup>2</sup> = 29%							
Test for overall effect: $Z = 3.18$ (P = 0.001)						0.01 0.1 1 10 100	
	rences: Chi <sup>2</sup> = 0.01. df	= 1 (P = 0	$(93) I^2 = 0^9$	%			MFPR higher-order to twin Ongoing triplet
rest for subgroup diffe		1.1 - 0		/0			



### RESULTS

- Thirty studies with a total of 9,811 women were included.
- MFPR from triplet to twin was associated with lower risk for HDP compared to ongoing triplets (OR 0.55, 95% CI 0.37-0.83, p=0.004).
- In a subgroup analysis the decreased risk of HDP was driven by GH, and PE was no longer significant (OR 0.34, 95% CI, 0.17-0.70, p=0.004 and OR 0.64, 95% CI 0.38-1.09, p=0.10, respectively).
- HDP was also significantly lower after MFPR from all higher-order (including triplets) to twin compared to ongoing triplets (OR 0.55, 95% CI, 0.38-0.79, p=0.001).
- In a subgroup analysis the decreased risk of HDP was driven by PE, and GH was no longer significant (OR 0.55, 95% CI 0.32-0.92, p=0.02 and OR 0.55, 95% CI 0.28-1.06, p=0.08, respectively).

### DISCUSSION

- This meta-analysis suggests that MFPR in women with triplet and higher-order multifetal pregnancies decreases the risk of HDP compared to women with ongoing triplet pregnancies.
- For MFPR from triplet to twin versus ongoing triplets this is driven by GH and for MFPR from higher-order to twin versus ongoing triplets this is driven by PE.
- These data can be used in the decisionmaking process of MFPR, in which the individual risk factors of HDP can be taken into account.