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## Hypertensive Disorders in Twin Pregnancies

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**Abstract.** This study investigates the influence of hypertensive disorders on twin pregnancies for an unselected, population-based series. Between 1986 and 1991, out of a total of 56,381, 766 (1.3%) were twin deliveries at our institution, the only tertiary care hospital serving a population of about 400,000 inhabitants. The incidence of hypertensive disorders was significantly higher in twin gestations than in singleton pregnancies, at 3437/55,615 (6.2%) vs 85/766 (11.1%) ( $p < 0.001$ , OR = 1.8, 95% CI = 1.4-2.3). Hypertensive disorders were significantly higher in twin as compared to singleton pregnancies, regardless of parity, and even after adjusting for maternal age. More instrumental or surgical deliveries were needed when pregnancies were complicated by hypertension, in twin as well as singleton gestations. Despite the association between prematurity and hypertensive disorders, and prematurity and perinatal mortality, no significant difference was found in perinatal mortality between hypertensive and normotensive twin pregnancies. The neonatal death-rate in normotensive and hypertensive twin pregnancies (3.7% and 3.5% respectively) was higher than that of stillbirths (respectively 2.3% and 0%).

**Key words:** Twin pregnancies, Hypertension

## INTRODUCTION

The association between multiple pregnancy and an increase in hypertensive disorders has been described [1], [3]-[5], [7]. The greater predisposition of women with twin pregnancies to hypertensive disorders has been commonly attributed to hyperplacentalis [7]. However, the rates reported in previous studies vary greatly. While the incidence of preeclampsia was 25.9% in a series of 642 twin pregnancies [7], it was only 14.5% in a recent study of 488 pregnancies [5]. Similarly, the frequency of hypertensive disorders

was 12.5% in a recent Israeli study [1]. In addition to the risk to twin pregnancy per se, which hypertensive disorders entail, they may further impair maternal and fetal outcome. Little data is presently available on neonatal outcome in twin pregnancies complicated by hypertensive disorders, however. The aim of this study was to determine the rate of common obstetric complications in twin gestations affected by hypertensive disorders.

## MATERIALS AND METHODS

Computerized data on the obstetric population was obtained for the six year period between 1986-1991. All the births occurred in the Soroka Medical Center, the only tertiary care hospital in the southern area of Israel. The computerized discharge records are routinely completed in a consistent and unified manner by the medical team attending the parturients.

Hypertensive disorders, with or without proteinuria were defined as **mild hypertension** when the gravida's blood pressure was measured 140/90 to 159/109 mmHg, twice, 6 hours apart, in the second half of pregnancy **Severe hypertension** was defined as a blood pressure of  $\geq 160/110$  mm Hg, measured twice, six hours apart, in the second half of pregnancy. **Chronic hypertension** was defined as hypertension found before gestation, or during the first half of pregnancy. **Superimposed hypertension** was defined as an increase of 30 or 15 mmHg in systolic or diastolic blood pressure measurements, respectively, in a chronic hypertensive patient during the second half of pregnancy. Blood pressure was measured with the gravida in the supine position and Korotkow IV was taken as the low value. The associations of hypertensive disorders in singleton and twin pregnancies were analyzed in relation to the following variables: maternal age, gravidity, parity, gestational age at delivery, and mode of delivery. Obstetrical complications such as abruptio placenta, placenta previa, cord prolapse, intrauterine growth retardation (IUGR), and premature rupture of membranes, were also determined and compared between both groups.

Categorical variables were analyzed using the chi-square of Fisher's exact test, as appropriate. Continuous variables were analyzed using the Student's T-test for comparison of two groups, or analysis of variance for three groups or more. When the ANOVA was statistically significant ( $p < 0.05$ ), the Scheffe test was used a posteriori, to compare between pairs of means. Relative risks (RR) and 95% confidence intervals (95% CI) were computed, comparing twin to singleton deliveries. Age adjusted relative risks were computed using the Mantel-Haenszel method, after stratifying rates of hypertensive disorders in singleton and twin births into five age groups:  $\leq 20$  years, 21-25, 26-30, 31-35, and delivering mothers who were 36 years or older. The adjustment was performed separately for primiparous and multiparous women.

## RESULTS

During the study period, among a total of 56,381 deliveries, there were 766 twin deliveries. The frequency of hypertensive disorders was significantly higher in twin pregnancies

than in singleton pregnancies, being 11.1% and 6.2% in twins and singletons, respectively. Maternal age was significantly higher in the group of women with twin pregnancies, when compared with that of women with singleton pregnancies ( $p < 0.0001$ ) (Table 1). In singleton pregnancies, maternal age was also significantly higher in hypertensive than in normotensive mothers; ( $p < 0.0001$ ), but no difference was found in maternal age between normotensive and hypertensive twin pregnancies. After controlling for maternal age, the risk of hypertension in twin pregnancy was evident [RR 1.83 (95% CI = 1.45-2.33)  $p < 0.00001$ ]. Gravity and parity were significantly higher in twin than in singleton pregnancies ( $p < 0.05$ ) (Table 1). Statistically significant difference was also found in gestational age at delivery between singleton and twin pregnancies ( $p < 0.0001$ ), as well as between singleton normotensive and hypertensive pregnancies ( $p < 0.0001$ ). No difference was found in gestational age at delivery between normotensive and hypertensive twins (Table 1).

**Table 1 - Mean values and Standard Deviation (in brackets) of selected obstetric characteristics in singleton and twin pregnancies by hypertensive disease**

	All	Normot	Hypert	p value	
				a	b
<i>Maternal age (years)</i>					
Singleton	28.1 (6.4)	28.0 (6.3)	29.5 (7.1)	< 0.0001	< 0.0001
Twin	29.4 (6.7)	29.3 (6.7)	29.5 (6.2)	ns	
<i>Gravity</i>					
Singleton	3.9 (2.8)	3.8 (2.8)	4.2 (3.6)	< 0.0001	< 0.05
Twin	4.1 (3.0)	4.1 (2.9)	4.2 (4.0)	ns	
<i>Parity</i>					
Singleton	3.4 (2.6)	3.4 (2.5)	3.7 (3.2)	< 0.0001	< 0.05
Twin	3.6 (2.8)	3.6 (2.7)	3.7 (3.5)	ns	
<i>Gestational age at delivery (weeks)</i>					
Singleton	39.2 (2.3)	39.3 (2.2)	38.6 (2.5)	< 0.0001	< 0.0001
Twin	36.1 (3.3)	36.0 (3.4)	36.3 (3.1)	ns	

**Legend**

- Normot = Normotensive women
- Hypert = Hypertensive patients
- a = Comparison between normotensive and hypertensive mothers
- b = Comparison between singleton and twin pregnancies

Hypertensive disorder rates in primiparae were 8.7% in singleton and 20.2% in twin deliveries ( $p < 0.0001$ ), compared to rates of 4.6% and 7.1% ( $p = 0.0166$ ) for women with 2-5 deliveries. In the group of women with 6 or more deliveries, the rates were 8.3% vs 13.1% for singletons and twins respectively ( $p = 0.0553$ ). And comparing the incidence of all hypertensive disorders in twin pregnancies between primiparous and multiparous women, a significantly higher rate of hypertensive disorders was found in primiparous twin pregnancies (22.5%) than in multiparous twin pregnancies (8.5%) [RR = 3.13 (95% CI = 1.88-5.22),  $p < 0.0001$ ].

Table 2 displays the relative risk of hypertensive disorders in primiparous and multiparous women, comparing twin pregnancies to singleton deliveries, adjusted for maternal age. The relative risk for mild and severe hypertension was significantly higher for twin pregnancies in primiparous as well as in multiparous women. When chronic, complicated with superimposed hypertension was examined, the relative risk was only significantly higher for primiparous women with twin pregnancies.

**Table 2 - Rates (in percent) of hypertensive disorders and age-adjusted relative risks of hypertension in twin vs singleton deliveries\***

Hypertensive disorder n =	Primiparous					Multiparous				
	Twin		Singleton			Twin		Singleton		
	142	10,985	Rate	Rate	RR (95% CI) p value	624	44,013	Rate	Rate	RR (95% CI) p value
Mild	13.7	5.9	2.7	(1.9-3.9)	<0.0001	5.7	3.1	1.8	(1.4-2.4)	<0.0001
Severe	6.3	1.9	4.0	(2.3-6.7)	<0.0001	1.6	0.7	2.2	(1.4-3.6)	0.0007
Chronic with superimposed	2.1	0.6	3.3	(1.3-8.3)	0.0106	1.3	1.7	0.7	(0.4-1.1)	ns

\* Relative risks (RR) and 95% confidence intervals (95% CI) calculated using the Mantel-Haenszel method are presented by parity.

When specific hypertensive disorders in twin pregnancies are examined (Figure), the greatest difference between primiparous and multiparous women is that seen for severe hypertension. Mild hypertension is about twice as frequent in primiparous women, while superimposed hypertension is only marginally increased.

The frequency of intrauterine growth retardation (IUGR) was higher in twins of hypertensive than normotensive mothers, but this increase was not statistically significant. Singleton newborns of hypertensive mothers, on the other hand, were significantly more often intrauterine growth retarded than singletons of normotensive mothers. However, all IUGR rates in twins, regardless of hypertensive disorder, were considerably higher than in singleton births (Table 3). Premature rupture of membranes was found significantly more often in twins as compared with singleton pregnancies, without any relation to hypertension (Table 3). Separation of a normally inserted placenta (abruptio placentae) was diagnosed significantly more frequently in hypertensive than

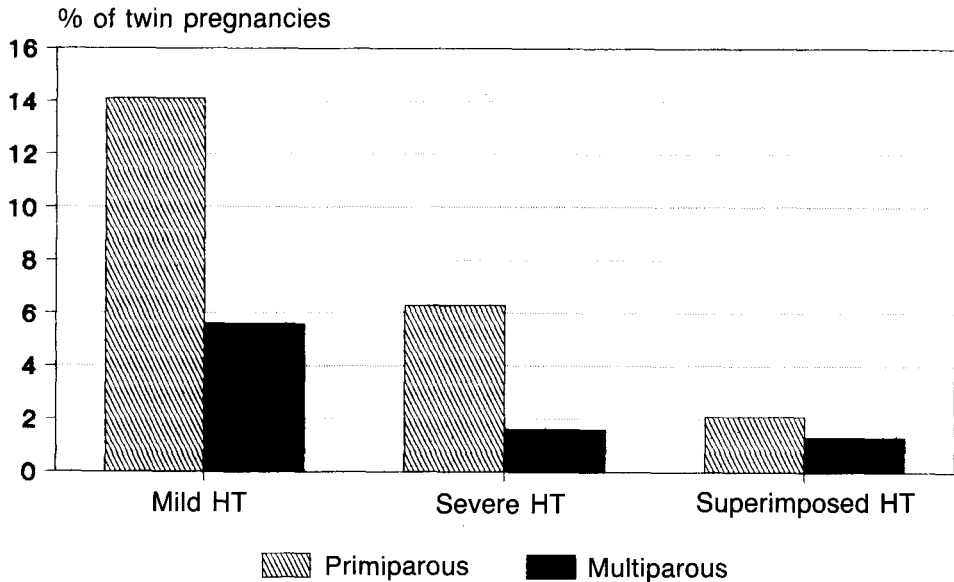


Fig. Parity and hypertensive disorders in twin pregnancies.

in normotensive singleton pregnancies, and virtually no difference was observed in twin gestations (Table 3). On the other hand, cord prolapse was more common in deliveries of twins born to normotensive mothers (Table 3).

The incidence of IUGR, premature rupture of membranes, abruptio placentae and cord prolapse was rather similar in normotensive and hypertensive twin pregnancies. However, these conditions were significantly more frequent in twin than in singleton pregnancies, presenting respectively the following incidence rates. IUGR: 13.0% vs 2.8% ( $p < 0.0001$ ); premature rupture of membranes: 4.2% vs 3.2% ( $p = 0.003$ ); abruptio placentae: 1.5% vs 0.6% ( $p < 0.0001$ ); cord prolapse 1.8% vs 0.3% ( $p < 0.0001$ ). There was no significant association of hypertensive disorders with placenta previa in either singleton or twin pregnancies.

An analysis of the mode of delivery in singleton and twin pregnancies complicated by hypertensive disorders, compared to normotensive pregnancies, shows that the overall frequency of operative deliveries was significantly higher in hypertensive than in normotensive singleton and twin pregnancies (Table 4). The birthweight of singletons born to hypertensive women was significantly lower than that of those born to normotensive women [(3,027 ± 685 vs 3,182 ± 541) ( $p < 0.0001$ ), respectively]. No significant difference was found between twin birthweights in hypertensive (2,340 ± 596) and normotensive mothers (2,237 ± 612).

Perinatal mortality was significantly higher in the infants of hypertensive than normotensive women with singleton pregnancies ( $p < 0.0001$ ). In twin pregnancies, perinatal mortality in the group of hypertensive twins was found to be half of that in the group of normotensive twins (Table 5). Rates of hypertension in different-sex twin pregnancies (10.9%) did not differ from those in same-sex twin pregnancies (11.2%).

**Table 3 - Selected obstetric complications associated with hypertensive disorders in singleton and twin pregnancies**

	n =	Singleton		Twins	
		Normot 52,178	Hypert 3,437	Normot 1,362	Hypert 170
IUGR		1,333	243	174	26
	%	2.6	7.0	12.8	15.3
	p value	<0.0001		ns	
PROM		1,674	97	56	8
	%	3.2	2.8	4.1	4.7
	p value	ns		ns	
Abruptio placentae		293	52	20	3
	%	0.6	1.5	1.5	1.8
	p value	<0.0001		ns	
Cord prolapse		174	13	27	1
	%	0.3	0.4	2.0	0.6
	p value	ns		ns	

**Legend**

Normot = Normotensive women

Hypert = Hypertensive patients

IUGR = Intrauterine growth retardation

PROM = Premature rupture of membranes

Proteinuria was found in 57.9% of hypertensive twin pregnancies, as compared with 54.4% of singleton hypertensive pregnancies (40/69 vs 53/97). In addition, the rate of monozygotic twinning in hypertensive disorders (16.9%), does not differ significantly from the 10% of expected monozygotic twins in normal pregnancies.

**DISCUSSION**

This study confirms the generally accepted clinical feature of significantly higher rates of hypertensive disorders in twin than in singleton pregnancies [8]. Those investigating twin pregnancies consider hypertensive disorders as one of the main complications, and the incidence found by the different authors ranges between 25.9% [7] and 12.5% [1]. Moreover, it has been stated that as many as 40% of twin pregnancies are complicated by hypertension, and that hypertension is more common, occurs earlier and is more severe in twin than in singleton pregnancies [4]. Our study shows an incidence of 11.1%, which is almost double that of hypertensive disorders in our singleton obstetric population.

**Table 4 - Mode of delivery associated with hypertensive disorders in singleton and twin pregnancies**

	n =	Singleton		Twins	
		Normot	Hypert	Normot	Hypert
Spontaneous		44,305	2,492	626	57
%		84.9	72.5	46.0	33.5
Vacuum extraction		1,117	110	15	3
%		2.1	3.2	1.1	1.8
Classic CS		220	25	16	0
%		0.4	0.7	1.2	0.0
Low segment CS		4,240	674	478	86
%		8.1	19.6	35.1	50.6
Other		2,296	136	227	24
%		4.5	4.0	16.7	14.1
p value		<0.0001		= 0.0017	

**Legend**

Normot = Normotensive women

Hypert = Hypertensive patients

CS = Cesarean section

It should be stressed that after controlling for maternal age, the relative risk of hypertensive disorders in the case of twin pregnancy is almost twice that in singleton pregnancies, suggesting that twinning and not maternal age per se is causally related to hypertension in pregnancy. In addition, the risk of hypertensive disorders in twin pregnancies is higher, irrespective of parity. Our data support the fact that also primiparity alone, in addition to twinning, constitutes a risk factor for hypertensive disorders (Figure). Early delivery in twin pregnancies reduces the time period during which twin fetuses are subjected to the growth-retarding effect of hypertension. Thus, a difference in the incidence of IUGR in normotensive versus hypertensive twins is most probably prevented (Table 3). However, the fact that a higher rate of intrauterine growth retardation was found in hypertensive twins than in hypertensive singletons, lends support to the hypothesis that a preceding utero-placental ischaemia impairs fetal growth before hypertension has been diagnosed [7].

As expected, abruptio placentae was diagnosed more frequently in women with hypertensive disease than in normotensive women. It may be that the small numbers of cases recorded in my study did not reveal a significant difference between the frequency of abruptio placentae in hypertensive versus normotensive twins. Two earlier studies

**Table 5 - Perinatal mortality in hypertensive singleton and twin pregnancies**

	n =	Singleton		Twins	
		Normot	Hypert	Normot	Hypert
		52,178	3,437	1,362	170
APD		350	47	27	0
	%	0.7	1.4	2.0	0.0
	p value	<0.0001		ns	
IPD		79	6	5	0
	%	0.2	0.2	0.4	0.0
	p value	ns		ns	
PPD		411	37	51	6
	%	0.8	1.1	3.7	3.5
	p value	ns		ns	
<i>Total PM</i>		840	90	83	6
	%	1.6	2.6	6.1	3.5
	p value	<0.0001		ns	

**Legend**

Normot = Normotensive  
 Hypert = Hypertensive  
 APD = Ante-partum death  
 IPD = Intra-partum death  
 PPD = Post-partum death (until 7 days after birth)  
 PM = Perinatal mortality

both found that the mean birthweight of twin pregnancies complicated by pre-eclampsia was lower than that of normotensive twin pregnancies [1], [7]. However, our data revealed no difference in the mean birthweight between normotensive and hypertensive twins. Younger parturients and the small number of chronically hypertensive patients may have contributed to this difference.

Spontaneous delivery in hypertensive twin pregnancies was seen in only one third of the cases. Thus, hypertensive disease was a risk factor at the delivery of twin gestations. A more-than-twofold increase in surgical deliveries occurred in hypertensive twin compared to hypertensive singleton births. Total perinatal mortality increases greatly (three to fourfold) in twin versus singleton pregnancies [2]. While the rate of perinatal mortality was significantly higher in hypertensive versus normotensive singletons, hypertensive twins showed only half the perinatal mortality rate of normotensive twins. However, these data should be approached with reservation. Despite the large series we are presenting, the low mortality rates being achieved today makes the comparison between twin subsets difficult. Women with hypertensive disorders who are carrying twins are



generally hospitalized, while most normotensive women who are pregnant with twins remain ambulatory. The overall perinatal mortality rate of the first twin was found to be lower than that of the second twin, and similar results have also been reported elsewhere [5].

We have shown that twin pregnancies are an independent risk factor for hypertensive disorders. Uterine over-distension is a known risk factor for hypertension. It was postulated that defective hypertrophy of the uterine artery in some pregnancies may give way to stretching, distortion and narrowing of the arterial lumen [6]. The rate of growth of the uterus in pregnant women may not be synchronous with the expected hypertrophy of the uterine artery, thus jeopardizing the blood flow in branches such as the arcuate and spiral arteries. It was hypothesized that this blood flow disturbance may lead to subsequent placental hypoxia, which is associated with hypertension.

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