

## Lipids in Hypertensive Disorders of Pregnancy and Birth Weight

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### Abstract

Hypertensive Disorders of Pregnancy affect growth of fetus, birth weight too. However all babies are not small. This might have something to do with lipids.

**Objective:** Present study was to study serum lipid levels in normal pregnant, women with HDsP, specially lipid abnormalities in HDsP and birth weight of baby.

**Materials and methods:** Prospective study was carried out with singleton pregnancy, gestational age more than 20 weeks with HDsP. Normotensive pregnant women, matched for age, (+2) parity (+1), gestational age (+2 weeks) were controls. Fasting serum lipids, cholesterol, triglycerides, high density lipoproteins (HDL), low density lipoproteins (LDL), very low density lipoproteins (VLDL) were estimated at entry, repeated 7 days. Criterion for small for gestation weight was less than 2500 gms birth weight of >37 weeks babies. Preterm were excluded for analysis.

**Results:** During study there were 7233 births, 964 had HDsP (13.32%), 635 (66%) term (>37 weeks) pregnancy. Of 451 women with mild gestational hypertension (GH), 425 had abnormal lipids, 117 (27.52%) of them, of 26 with normal lipids, 23.07% had SGA babies, more babies SGA with higher LDL, VLDL, Tri glycerides, lower HDL. Among 58 term cases with severe GH, 50 had abnormal lipid levels, 8 (16%) and of 8 with normal lipids, one (12.5%) had SGA baby, more babies SGA with abnormal lipids. Among 65 of term gestation with mild PE, 48 had abnormal lipids, 17 (35.41%) and of 17 with normal lipids 4 (23.52%) had SGA babies with abnormal lipids, more SGA babies with abnormal lipids. With severe PE, all 44 had some lipid abnormality, 59% had SGA babies. All 17 with eclampsia at term had abnormal lipids, 16 (94.11%) had SGA babies. However in all categories difference was statistically insignificant.

**Conclusion:** Lipid abnormalities were present in quite a few cases of HDsP and when present affected baby weight. A lot of more research is needed.

**Keywords:** Hypertensive disorders of pregnancy lipids; Birth weight

### Objectives

The present study has been done to study the serum lipid levels in normal pregnant women and in women with HDsP with special reference to lipid abnormalities in women with HDsP and birth weight of the baby in these women.

### Introduction

#### Background

Hypertensive disorders of pregnancy (HDsP) complicate 2-22% of pregnancies [1-3] and contribute to a lot of maternal, fetal, neonatal morbidity and mortality [4-7]. HDsP affect the growth of the fetus, so birth weight is affected, however all babies are not small. This might have something to do with lipids [7-10]. As such during pregnancy lipid metabolism is altered with hyperlipidemia, more marked towards term [11-15]. The exact mechanisms underlying these alterations are not clear [15-20]. During early pregnancy, lipid metabolism changes under hormonal control [21-23]. In complicated pregnancies, there might be defects in the lipid metabolism with hyperlipidemia [24]. There is increase in the hepatic lipase activity and decrease in lipoprotein lipase activity [25]. Also there is increased synthesis of triglycerides at hepatic level with accumulation of triglycerides in plasma. Hypertriglyceridemia and other lipid abnormalities have positive relationship with HDsP [23]. Role of lipids in the pathogenesis of HDsP lipid abnormalities, effects on mother and baby are not well understood, so research continues.

### Materials and Methods

The present prospective study was carried out at a rural institute over a period of two years. Pregnant women with singleton pregnancy, gestational age more than 20 weeks with hypertensive disorders admitted to the maternity wards were included in the study after informed consent. Women with pre pregnancy hypertension, diabetes, renal, coagulation disorders, epilepsy or any other medical disorder were excluded. Preeclampsia (PE) was diagnosed if hypertension was associated with proteinuria, and eclampsia when preeclampsia was associated with seizures. Normotensive pregnant women matched for age, parity (+1) and gestational age (+2 weeks) were the controls. Fasting serum lipids, cholesterol, triglycerides, high density lipoproteins (HDL), low density lipoproteins (LDL) and very low density lipoproteins (VLDL) levels were estimated at entry and repeated every 7 days. The criterion for the LBW for the newborn was,

at completed 37 weeks and beyond birth weight less than 2500 gms. All the preterm deliveries in all the groups were excluded.

## Results

During the study period there were 7233 births, of which 964 women had HDsP, 13.32% of births. Of the 964 women, 635 (66%) had term (>37 weeks) and 34% had preterm gestation. Of the 964 women 609 (63.17%) had mild gestational hypertension (GH) [BP 140/90 or more but less than 160/110], 85 (8.60%) had severe GH (BP160/110 or

more), 168 (11.20%) mild PE (mild hypertension with proteinuria), 150 (11.92%) had severe PE and 49 (5.08%) women had eclampsia (GH/PE with convulsions and /or coma). The mean cholesterol level was 236.2 mg/dl in women with HDsP compared to 141.2 mg/dl among normotensive pregnant women, the mean triglyceride level was 277.8 mg/dl among study subjects compared to 142.3 mg/dl among normal pregnant women, the mean LDL level among the women with hypertensive disorders was 142.93 mg/dl compared to 117.4 mg/dl among normal case.

Parity	Lipid Levels	Period of Gestation			Total
		<34wks	34-<37	>37 wks	
Primigravida (785)	C<200	32	219	404	655
	C>200	1	6	123	130
	H>30	33	223	493	749
	H<30		2	34	36
	T<150	31	212	376	619
	T>150	2	13	151	166
	L<160	33	222	464	719
	L>160		3	63	66
	V<30	32	219	409	660
	V>30	1	6	118	125
<b>T</b>		33	225	527	785
Multigravida (179)	C<200	12	49	90	144
	C>200	5	5	22	28
	H>30	13	52	106	171
	H<30	4	2	6	8
	T<150	12	38	106	163
	T>150	15	16	36	46
	L<160	13	53	105	171
	L>160	4	1	7	8
	V<30	13	48	88	149
	V>30	4	6	14	20
<b>Total</b>		17	54	112	179
<b>Grand Total</b>		50	279	635	964

P-Parity; T-Total; GT-Grand Total; LL-Lipid Levels; C<200-Cholesterol <200 mg/dl; C>200-Cholesterol >200 mg/dl; H<30-HDL<30mg/dl; H>30-HDL>30mg/dl; T<150-Triglyceride<150mg/dl; T>150-Triglyceride>150mg/dl; L<160-LDL <160 mg/dl; L>160-LDL >160 mg/dl; V<30-VLDL<30mg/dl; V>30-VLDL>30mg/dl

**Table 1:** Parity, gestational age lipid levels among normotensive women.

Mean VLDL level among hypertensive women was 77.2 mg/dl compared to 39.6 mg/dl among controls, while the mean HDL level

among women with hypertensive disorders was 41.5 mg/dl compared to 51.2 mg/dl among controls (Tables 1 and 2).

P	Lipid Levels	Period of Gestation														
		< 34 Weeks (105)					35-37 weeks (224)					>37 weeks (635)				
		Mild PIH	S PIH	MPE	S PE	Ecl	Mild PIH	S PIH	MPE	SPE	Ecl	Mild PIH	S PIH	MPE	SPE	Ecl
N (785)	C<200	23	1	2		1	51	1	2	2		190	7	14	3	
	C>200	16	1	3	10	8	44	8	15	36	11	220	33	28	34	12
	H>30	37	1	3	8	4	90	6	16	29	8	378	38	42	5	2
	H<30	2	1	2	2	5	5	3	1	9	3	32	2		32	10
	T<150	3					4		2	1		37		4		
	T>150	36	2	5	10	9	91	9	15	37	11	373	40	38	37	12
	L<160	30	1	3	3	2	88	5	7	12	3	371	24	30	15	1
	L>160	9	1	2	7	7	7	4	10	26	8	39	16	12	22	11
	V<30	5	1	1	1	1	7	4	3	1		25	2	4	2	
	V>30	34	1	4	9	8	88	5	14	37	11	385	38	38	35	12
<b>TOT</b>		39	2	5	10	9	95	9	17	38	11	410	40	42	37	12
M (179)	C<200	4		1	1		3	1	6			15	9	3		1
	C>200	6	4	6	14	5	12	9	8	8	7	26	9	20	7	4
	H>30	1	4	5	12	4	14	9	14	8	5	37	16	21	4	
	H<30	9		2	3	1	1	1			2	4	2	2	3	5
	T<150	5		4	3		1		1	2		5	2	1		
	T>150	5	4	3	12	5	14	10	13	6	7	34	16	22	7	5
	L<160	7		2	2		10	7	12	2		32	13	15	2	3
	L>160	3	4	5	13	5	5	3	2	6	7	9	5	8	5	2
	V<30	4		2	2		6	3	10	2		1	6	2	1	1
	V>30	6	4	5	13	5	7	6	4	3	7	32	12	17	6	4
<b>TOTAL</b>		10	4	7	15	5	15	10	14	8	7	41	18	23	7	5
<b>Grand Total</b>		49	6	12	25	14	110	19	31	46	18	451	58	65	44	17

P-Parity; N-Nulliparous; M-Multiparous; C-Cholesterol (<200, > 200); H-HDL (<30, >30); T-Triglyceride (<150, >150); L-LDL (<160, >160); V-VLDL (<30, >30)

**Table 2:** Distribution of parity, gestational age and severity of hypertensive disorder with lipid levels.

Of the 609 women with mild GH, 48 had gestational age of 28-34 weeks, twenty two of 48 (45.83%) of them had elevated cholesterol, 2 (4.16%) low HDL, 41(65.42%) elevated triglycerides, 11 (22.91%) elevated LDL and 40 (63.34%) elevated VLDL of the 110 women between 35-37 weeks pregnancy with mild GH, 56 (50.90%) had elevated cholesterol, 6 (5.45%) low HDL, 105 (95.45%) elevated triglycerides, 12 (10.90%) elevated LDL, and 95 (86.36%) had elevated VLDL. Of the 451 women with gestational age >37 weeks, 425 (94.23%) had elevated VLDL, 246 (54.54%) elevated cholesterol, 4 (0.88%) low HDL 407 (90.24%) had elevated triglycerides and 48 (10.64%) had elevated LDL.

After excluding all the preterm deliveries from the MGH group 451 women were of term gestation, of which 425 women had abnormal lipid levels. Of the 425 women with abnormal lipids 117 (27.52%) had SGA babies and of 26 mothers with normal lipids 6 (23.07%) had SGA babies, more babies SGA with higher LDL VLDL, TGs but difference was insignificant.

Amongst the 85 women with severe GH, 8 were of the gestational age between 28-34 weeks, among whom 5 (62.5%) had elevated cholesterol, one (12.5%) had low HDL, 6 (75%) had elevated triglycerides, 5 (62.5%) had elevated VLDL and one (12.5%) had low HDL. Nineteen women with 35-37 weeks pregnancy, 17 (89.47%) had elevated cholesterol, all 19 had elevated triglycerides, 7 (36.84%)

elevated LDL and 11 (57.89%) had elevated VLDL and 4 (21.05%) low HDL of 58 women were of >37 weeks gestation, 42 (72.41%) had elevated cholesterol, 4 (6.89%) had low HDL, 46 (79.31%) elevated triglycerides, 21(36.20%) had elevated LDL and 50 (86.20%) had elevated VLDL. Among term 58 cases, 50 (86.2%) women had abnormal lipid levels, of which 8 (16%) mothers had SGA babies and of 8 mothers with normal lipid level, one (12.5%) had SGA baby, more babies were SGA with abnormal lipids however this difference was statistically insignificant.

Among 168 women with mild Pre eclampsia 72 were of 28-34 weeks, 9 (12.5%) of them had elevated cholesterol, 8 (11.10%) had elevated triglycerides, 7 (9.72%) had elevated LDL, 9 (12.5%) had elevated VLDL and 4 (5.55%) had low HDL. Of thirty one women out of 168 with 35-37 weeks gestation, 23 (74.19%) had elevated cholesterol, one (3.22%) had low HDL, 28 (90.32%) elevated triglycerides, 12 (38.70%) elevated LDL and 18 (58.06%) elevated VLDL. Of sixty five of 168 women with mild preeclampsia of more than 37 weeks or more gestation, 48 (73.84%) had elevated cholesterol, 2 (3.07%) low HDL, 60 (92.30%) had elevated triglycerides, 20 (30.76%) elevated LDL and 55 (84.61%) elevated VLDL. Among 65 women of term gestation 48 had abnormal lipids, of which 17 (35.41%) mothers had SGA babies and of 17 mothers with normal lipids 4 (23.52%) mothers had SGA babies, more babies SGA but the difference was insignificant.

Of 240 women with severe preeclampsia, 150 were pf > 28-<34 weeks pregnancy 24 (16%) had elevated cholesterol, 22 (14.66%) had elevated triglycerides, 20 (13.33%) had elevated LDL 22 (14.66%) had elevated HDL and 5 (3.33%) had below normal HDL. Forty six of these 240 with 35-37 weeks pregnancy, 44 (95.65%) had elevated cholesterol, 43 (93.47%) had elevated triglycerides, 32 (69.56%) had elevated LDL, 40 (86.95%) elevated VLDL and 9 (19.56%) had below normal HDL. Of the 240 women with severe PE, 44 were of >37 weeks pregnancy, 41 (93.18%) had elevated cholesterol, all 44 had elevated triglycerides, 27 (61.36%) elevated LDL and 41 (93.18%) had elevated VLDL and 35 (79.54%) had below normal HDL, no one had normal lipids level and 26 (59.09%) of them had SGA babies.

Of 49 women with eclampsia, 14 had 28-34 weeks of pregnancy 13 (92.85%) had elevated cholesterol, all had elevated triglycerides, 12 (85.60%) had elevated LDL and 13 (92.85%) elevated VLDL and 6 (42.85%) below normal HDL. Eighteen of 49 women with eclampsia with 34-37 weeks had elevated cholesterol, all had elevated triglycerides, 15 (83.33%) elevated LDL, all had elevated VLDL and 5 (27.77%) had below normal HDL. Seventeen of 49 women were >37 weeks pregnancy, 16 (94.11%) had elevated cholesterol, all had elevated triglycerides, 13 (76.47%) elevated LDL and 16 (94.11%) had elevated VLDL and 15 (88.23%) had below normal HDL. All the 17 women with eclampsia at term gestation had abnormal lipids, 16 (94.11%) of them had SGA babies (Table 3).

HDsP with >37 weeks gestation	Serum lipid Levels	No	SGA		TOTAL	
			No	%	No	%
MGH (451)	Normal	26	6	23.07	123	27.27
	Abnormal	425	117	27.52		
SGH (58)	Normal	8	1	12.5	9	15.51
	Abnormal	50	8	16		
MPE(65)	Normal	17	4	23.52	21	32.3
	Abnormal	48	17	35.41		
SPE (44)	Normal	0	0	0	26	59.09
	Abnormal	44	26	59.09		
ECL (17)	Normal	0	0	0	16	94.11
	Abnormal	17	16	94.11		
TOTAL		635	195	30.7	195	30.7
		Normal	51	11	21.5	
		Abnormal	584	184	31.5	

MPIH: Mild Gestational Hypertension; SPIH: Severe Gestational Hypertension; MPE: Mild Preeclampsia; SPE: Severe Preeclampsia; ECL: Eclampsia; SGA: Small for Gestational Age.

**Table 3:** Severity of Hypertensive Disorders, serum lipid levels and birth weight in term delivered mothers.

## Discussion

Serum lipids have a direct effect on endothelial function, therefore dyslipidemia is linked to etiology of preeclampsia [26-29]. Though it was thought that higher maternal serum lipids in pregnancy lead to fetal macrosomia, but in hostile environment like HDsP, lipid

abnormalities might lead to small babies due to poor endothelial function [30]. One Asian study revealed that maternal serum lipids in pregnancy acted as an independent factor for PE in the later gestation which further affected the fetal outcome including birth weight [31]. One research highlighted the concept of physiological programming of the fetus in the mother with HDsP with abnormal lipids in which

hyperlipidemia reversed effect on the fetal weight when combined with HDsP. It was revealed that only hypertriglyceridemia caused macrosomia in the fetus of mothers with abnormal lipids [32]. On multivariate analysis it was revealed that increased birth weight correlated positively only with hypertriglyceridaemia [33]. Hence this opens a new area of research in the field of maternal lipids and intrauterine fetal growth. Research from Germany revealed that fetal triglycerides and cholesterol levels were negatively correlated with newborn birth weight. Triglycerides were significantly higher in SGA newborns compared with AGA. All these researchers opined that in hostile environment maternal, lipid levels could affect the fetal birth weight negatively.

In the present study the 964 hypertensive women, overall 627 (65%) had elevated cholesterol, 900 (93.4%) had elevated triglycerides, 260 (26.9%) had elevated LDL, 885 (91.8%) had elevated VLDL and 108 (11.2%) had HDL levels below normal compared to 158 (16.4%) elevated cholesterol, 212 (22%) with elevated triglycerides, 74 (7.7%) with elevated LDL, 145 (15%) elevated VLDL and 36 (3.7%) HDL was below normal among 964 normotensive women [34].

The mean cholesterol was 236.2 mg/dl in women with HDsP compared to 141.2 mg/dl among normotensive pregnant women ( $p < 0.05$ ), the mean triglycerides level was 277.8 mg/dl among study subjects and 142.3 mg/dl among normal pregnant women ( $p < 0.05$ ), the mean LDL level among the women with HDsP was 142.93 mg/dl compared to 117.4 mg/dl among normal cases ( $p < 0.05$ ). Mean VLDL level among HDsP was 77.2 mg/dl compared to 39.6 mg/dl among controls ( $p < 0.05$ ) while the mean HDL level among women with HDsP was 41.5 mg/dl compared to 51.2 mg/dl among controls ( $p > 0.05$ ). In the study by Kaaja et al. [35] women with HDsP exhibited 65% higher triglycerides and 18% lower HDL levels compared to controls. In another study, 40 women with PE had mean levels of cholesterol 220.9 mg/dl, triglycerides 260.83 mg/dl, LDL 124.6 mg/dl and HDL 44.17 mg/dl compared to mean cholesterol 187.6 mg/dl, triglycerides 196.6 mg/dl, LDL 94.2 mg/dl and HDL 53.7 mg/dl among normotensive pregnant women.

In the present study, of the total study subjects 964 cases of HDsP, 635 women had gestation  $> 37$  weeks. Of those 451 (71.02%) were of mild GH, 58 (9.13%) were severe GH, 65 (10.23%) were mild PE, 44 (6.92%) were severe PE and 17 (2.67%) were eclamptic mothers. Among these 635 mothers 51 (8.03%) had normal lipid levels and 585 (91.96%) had abnormal lipid levels. It shows the HDsP had a direct relationship with maternal serum lipid levels and birth weight too. Of the 51 mothers with normal lipid levels only 11 (21.56%) had SGA babies as compared to 584 mothers with abnormal lipid levels 184 (31.50%) had SGA babies (Table 3).

A lot of more research is needed in this aspect of HDsP.

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