



# Relationship of Severe Maternal Morbidity and Maternal Mortality to Serum Lipids in Hypertensive Disorders of Pregnancy

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## Abstract

**Background:** Hypertensive disorders of pregnancy (HDP) are associated with a large burden of maternal morbidity and mortality. Whether lipids affect the maternal outcome in these cases is not well known. Research goes on.

**Objective:** Study was conducted to know relationship between lipid abnormalities and severe morbidity, mortality in women with hypertensive disorders of pregnancy.

**Methodology:** In the present prospective study of women with singleton pregnancy of gestational 28 weeks and beyond with hypertensive disorders, fasting serum lipids, cholesterol, triglycerides, high density lipoproteins (HDL), low density lipoproteins (LDL) and very low density lipoproteins (VLDL) were estimated at entry and repeated every 7 days. Cases were observed for placental abruption, renal failure, pulmonary edema, HELLP (Hemolysis, Elevated liver enzymes, and low platelets), partial HELLP or post partum haemorrhage (PPH) and followed up till 7 days postpartum.

**Results:** Occurrence of maternal complications was significantly less ( $p < 0.001$ ) in women who had mild or severe PIH with normal serum lipid levels ( $p < 0.001$ ). In women with mild and severe preeclampsia with normal lipid levels the occurrence of the complications was significantly less ( $p < 0.001$ ). Only 2 women with eclampsia had normal lipid levels, hence comparison was not possible. Also there was linear relationship between period of gestation, serum lipid abnormalities and severity of maternal morbidities. Between the gestation period from 28-34 weeks, out of 292 women, 167 (57.19%) women had lipid abnormalities compared to 222 (99.10%) of 224 women between gestational age 34-37 weeks. Of the 964 women with hypertensive disease, four (0.41%) women died. Maternal Mortality Ratio (MMR) was 465.65 amongst HDP, 28.6% of the overall maternal mortality during the study period. Overall MMR during the study period was 200.54. MMR without hypertensive disorders was 163.34. Four women who died had deranged lipids

**Conclusion:** As observed dyslipidemia and severity of hypertensive disorders of pregnancy and complications are closely associated. Further research is needed to uncover these associations.

**Keywords:** Hypertensive disorders; Lipid derangement; Severe maternal morbidity and mortality.

## Introduction

Hypertensive disorders of pregnancy (HDP) are associated with a large burden of maternal morbidity and mortality Roberts [1], Dekkar [2], Farrokh-Eslamlou et al. [3], Bauserman et al. [4], Soni-Trinidad et al. [5] due to the disease itself or the consequences and interventions. In spite of being common disorders, HDP are not very well understood as to why some mothers do well and others do not. Among many causative

factors, serum lipids are believed to play an active role in the etiopathogenesis of hypertensive disorders of pregnancy Boden [6], Wakatsuki et al. [7], Herrera [8], Lain et al. [9], Herrera et al. [10], Nickens et al. [11] and may be affect the outcome too. HDP are known to be associated with dyslipidemia, placental dysfunction and endothelial cell activation. Dukić et al. [12], Stocks [13], Szpera-Gozdziejewicz et al. [14] whether lipids affect

the maternal outcome in these cases is not well known and research goes on.

## Objective

Study was conducted to know the relationship between lipid abnormalities and maternal morbidity and mortality in women with hypertensive disorders of pregnancy.

## Material and Methods

The present prospective study of women with singleton pregnancy of gestational age 28 weeks and beyond with pregnancy induced hypertension (PIH- hypertension systolic blood pressure 140, diastolic 90 or more) or preeclampsia [with proteinuria of more than 300mg/l in 24 hrs or 30 mg/dl (1+ dipstick) detected in random urine] or eclampsia (hypertension associated with seizures non-attributable to any other cause) was carried out over a period of two years at a rural institute after taking informed consent.

PIH and preeclampsia were further subdivided into mild (diastolic Blood Pressure 90-110 mm Hg or less), and severe (diastolic BP >110 mm Hg). Fasting serum lipids, cholesterol, triglycerides, high density lipoproteins (HDL), low density lipoproteins (LDL) and very low density lipoproteins (VLDL) were estimated at entry and repeated every 7 days.

Cases were observed for placental abruption, renal failure, pulmonary edema, HELLP (Hemolysis, Elevated liver enzymes, and low platelets), partial HELLP or post partum haemorrhage (PPH) and followed up till 7 days postpartum.

## Results

A total of 7233 births took place during the study period of which, 964 (13.32%) women had hypertensive disorders. 609 (63.17%) had Mild PIH, 83 (8.60%) severe PIH, 108 (11.20%) mild preeclampsia, 115, (11.92%) severe preeclampsia and 49 (5.08%) eclampsia. Of the 652 women with mild PIH, 325 had elevated cholesterol, 3 (0.92%) of them developed placental abruption, 10 (3.07%) PPH, and 3 (0.92%) had multiple problems (placental abruption, partial HELLP and PPH). Five hundred and ninety nine had elevated triglycerides, 3 (0.53%) of them developed placental abruption, one (0.17%) had partial HELLP, 9 (1.61%) had PPH and one (0.17%) had multiple problems. Seventy two women had elevated LDL, 3 (4.16%) of them had placental abruption, one (1.38%) partial HELLP and 5(6.94%) had PPH. One hundred fifty four women had elevated VLDL, of which 2 (1.29%) developed partial HELLP, 7(4.54%) PPH and one (0.64%) had multiple problems. Fourth four women had low serum HDL, 2 (4.54%) of them had placental abruption and 8 (18.18%) PPH. Overall of mild PIH cases, 7 (1.07%) had partial HELLP, 11 (1.68%) had placental abruption, 39(5.98%) had PPH, and 5 (0.76%) had multiple problems (including PPH, partial HELLP). The occurrence of maternal complications was significantly less ( $p<0.001$ ) in the women who had mild PIH with normal serum lipid levels.

Amongst the 67 women with severe PIH, 61 had elevated cholesterol, 6 (9.83%) of them had placental abruption, 3(4.91%) partial HELLP, 2(3.27%) HELLP, 5 (8.19%) PPH and 3 (4.91%) had multiple problems. Sixty one women had elevated triglycerides, ten (16.39%) of them had placental abruption, 2 (3.27%) partial HELLP, 2(3.27%) HELLP, 9 (14.75%) PPH and 6(9.83%) had multiple problems. Fifty nine women had elevated VLDL, of which 4 (6.77%) had placental abruption, one (1.69%) HELLP, 4 (6.77%) partial HELLP, 7 (11.86%) PPH and 2(3.38%) had multiple problems. Thirty two women had elevated LDL, of which, 9 (28.12%) had placental abruption, 11 (34.37%) partial HELLP, 2 (6.25%) HELLP, 6 (18.75%) PPH and 5 (15.62%) had multiple problems. All of them had normal HDL. Overall of 67 women with severe PIH, 29 (43.28%) had placental abruption, 20 (29.85%) partial HELLP, 7 (10.44%) HELLP, 27 (40.29%) had PPH and 16 (23.88%) had multiple problems. In the women with severe HDP with normal lipid levels, morbidities were significantly less ( $p<0.001$ ).

Among 91 women with mild preeclampsia, 89 had elevated cholesterol; seven of them (7.86%) had placental abruption, one (1.12%) PPH and 2 (2.24%) had multiple problems. Eighty three had elevated triglycerides, of which 7(8.43%) had placental abruption, 4 (4.81%) PPH and 4 (4.81%) had multiple problems. Thirty four had elevated LDL of which 4 (11.36%) had placental abruption, 3 (8.82%) PPH and one (2.94%) had multiple problems. Eighty three women had elevated VLDL of which 6 (7.22%) had placental abruption and 3 (3.61%) had PPH. Nine had lower serum HDL of which 3 (33.33%) had placental abruption, one (11.11%) partial HELLP, one (11.11%) HELLP, one (11.11%) renal failure and 3 (33.33%) had PPH. Overall 91 women with mild PE with abnormal lipid levels, 27 (29.67%) had placental abruption, one (1.09%) each had partial HELLP, HELLP and renal failure, 14 (15.38%) women had PPH and 7 (7.69%) women had multiple problems. In the women with mild preeclampsia and normal lipid levels, the occurrence of these complications was significantly less ( $p<0.001$ ).

Of all the 115 women with severe preeclampsia, 110 had elevated cholesterol, triglycerides and VLDL, 9 (8.18%) of them had placental abruption, 5 (4.54%) had partial HELLP, 6 (5.45%) HELLP, 10(9.09%) PPH, 3 (2.72%) pulmonary edema and one (1.36%) had renal failure. Thirty four women had elevated LDL, of which 4 (11.76%) had placental abruption, 5 (14.70%) had HELLP, 13 (38.23%) partial HELLP, 3 (8.82%) had PPH and 2 (5.88%) had renal failure. Twenty two women had low HDL 3 (12.5%) of them had HELLP, one (4.16%) placental abruption, 4 (16.66%) had PPH, one (4.16%) had pulmonary edema and 2(8.32%) had renal failure. Overall of 115 women with severe PE with lipid abnormalities, 14 (12.17%) had placental abruption, 18(15.65%) had partial HELLP, 14(12.17%) had HELLP, 17(14.78%) had PPH, 4 (3.47%) had pulmonary edema and 5 (4.34%) had renal failure. On comparing women having severe preeclampsia and normal lipid levels, complications were significantly less ( $p<0.001$ ). (Table 1& 2).

**Table 1:** Deranged Serum lipid levels and maternal morbidity.

Maternal Complications									
HDP	Serum Lipid levels	PA	PH	H	PE	RF	PPH	Multiple problems	Total morbidities
<b>MPIH</b>	↑Chol (325)	3	3	0	0	0	10	3	18
<b>609</b>	↑TG (559)	3	1	0	0	0	9	1	14
	↑LDL (72)	3	1	0	0	0	5	0	9
	↑VLDL(154)	0	2	0	0	0	7	1	10
	↓HDL(44)	2	0	0	0	0	8	0	10
	<b>TOTAL</b>	<b>11</b>	<b>7</b>	<b>0</b>	<b>0</b>	<b>0</b>	<b>39</b>	<b>5</b>	<b>62</b>
<b>SPIH</b>	↑Chol(61)	6	3	2	0	0	5	3	19
<b>83</b>	↑TG (81)	10	2	2	0	0	9	6	29
	↑LDL (32)	9	11	2	0	0	6	5	33
	↑VLDL (59)	4	4	1	0	0	7	2	18
	↓HDL	0	0	0	0	0	0	0	0
	<b>TOTAL</b>	<b>29</b>	<b>20</b>	<b>7</b>	<b>0</b>	<b>0</b>	<b>27</b>	<b>16</b>	<b>99</b>
<b>MPE</b>	↑Chol (89)	7	0	0	0	0	1	2	10
<b>108</b>	↑TG (93)	7	0	0	0	0	4	4	15
	↑LDL (34)	4	0	0	0	0	3	1	8
	↑VLDL (83)	6	0	0	0	0	3	0	9
	↓HDL (9)	3	1	1	0	1	3	0	9
	<b>TOTAL</b>	<b>27</b>	<b>1</b>	<b>1</b>	<b>0</b>	<b>1</b>	<b>14</b>	<b>7</b>	<b>51</b>
<b>SPE</b>	↑Chol (110)								
<b>115</b>	↑TG (110)								
	↑VLDL(110)								
	↑LDL (34)	4	13	5	0	2	3	0	27
	↓HDL (24)	1	0	3	1	2	4	0	11
	<b>TOTAL</b>	<b>14</b>	<b>18</b>	<b>14</b>	<b>4</b>	<b>5</b>	<b>17</b>	<b>0</b>	<b>72</b>
<b>ECL</b>	↑Chol (47)								
<b>49</b>	↑TG (47)								
	↑VLDL (47)								
	↓HDL (22)	6	1	3	1	2	6	0	19
	<b>TOTAL</b>	<b>12</b>	<b>3</b>	<b>5</b>	<b>2</b>	<b>4</b>	<b>10</b>	<b>0</b>	<b>36</b>
<b>964</b>	<b>GRAND TOTAL</b>	<b>93</b>	<b>49</b>	<b>27</b>	<b>6</b>	<b>10</b>	<b>107</b>	<b>28</b>	<b>320</b>

HDP- Hypertensive disorders of pregnancy, MPIH- Mild Pregnancy Induced Hypertension, SPIH- Severe Pregnancy Induced Hypertension, MPE- Mild Pre-eclampsia, SPE- Severe Preeclampsia, ECL- Eclampsia, PA- Placental Abruption, PH-Partial HELLP, H-HELLP, PE-Pulmonary Edema, RF-Renal Failure, PPH-Post Partum Hemorrhage.

**Table 2:** Severity of HDP and Maternal Morbidities.

Maternal Morbidities	Severity of Hypertensive disorders									
	MPIH n=652	%	SPIH n=67	%	MPE n=91	%	SPE n=115	%	ECL	%
									n=47	
Placental Abruption	11	1.68	29	43.28	27	29.67	14	12.17	12	25.53
Partial HELLP	7	1.07	20	29.85	1	1.09	18	15.65	3	6.38
HELLP	0	--	7	10.44	1	1.09	14	12.17	5	10.63
Renal Failure	0	--	0	--	1	1.09	5	4.34	4	8.51
Pulmonary Edema	0	--	0	--	0	--	4	3.47	2	4.25
Multiple Problems	4	0.61	16	23.88	7	7.69	0	--	0	--
PPH	39	5.98	27	40.29	14	15.38	17	14.78	10	21.27

MPIH- Mild Pregnancy Induced Hypertension, SPIH- Severe Pregnancy Induced Hypertension , MPE- Mild Pre-eclampsia, SPE- Severe Preeclampsia, ECL- Eclampsia, HELLP: Hemolysis, Elevated liver enzymes, Low platelets. PPH: Postpartum Haemorrhage.

Fourth seven women with eclampsia had elevated cholesterol, elevated triglycerides and elevated VLDL. 6 (12.76%) of them had placental abruption, 2 (4.25%) had partial HELLP, 2 had (4.25%) HELLP, 4 (8.51%) had PPH, one (2.12%) had pulmonary edema and 2 (4.25%) had renal failure. Twenty two women with eclampsia had low HDL 6 (27.27%) of them had placental abruption, 3 (13.63%) had HELLP, one (4.54%) had partial HELLP, 6 (27.27%) had PPH, one (4.54%) had pulmonary edema and 2 (9.09%) had renal failure. Of 47 women with eclampsia with deranged lipids, 12 (25.53%) had placental abruption, 3 (6.38%) had partial HELLP, 5 (10.63%) had HELLP, 10 (21.27%) had PPH, 2 (4.25%) had pulmonary edema and 4 (8.5%) women had renal failure. Only 2 women with eclampsia had normal lipid levels, hence comparison was not possible.

There was linear relationship between period of gestation, serum lipid abnormalities and severity of maternal morbidities. Between the gestation period from 28-34 weeks, out of 292 women, 167(57.19%) women had lipid abnormalities, compared to 222(99.10%) of 224 women between gestational age 34-37 and 432(68.03%) of 635women of gestation >37 weeks. Of the

964 women with hypertensive disease four (0.41%) women died. Amongst HDP cases. Maternal Mortality Ratio (MMR) was 465.65, 28.6% of the overall maternal mortality during the study period. Overall MMR during the study period was 200.54. MMR without these disorders was 163.34. All of the 4 women who died had deranged lipids; one was a 27 year old second para with severe preeclampsia at 28 weeks. She presented in coma and was diagnosed to have cerebral hemorrhage. She had elevated cholesterol, triglycerides. LDL, VLDL below normal HDL levels. The second woman was a 22 years primipara who had post partum eclampsia with HELLP, DIC and atonic PPH. She had elevated cholesterol, triglycerides, and LDL, VLDL and below normal HDL. The third case, a 20 years primipara with eclampsia, died due to intracranial hemorrhage and had elevated cholesterol, triglycerides, LDL, VLDL and normal HDL levels. Fourth woman was 24 years primipara with severe PIH with HELLP with DIC. She had elevated cholesterol, triglycerides, and LDL, VLDL below normal HDL levels. All the eclamptic women (2 of 4 who died) had severely deranged serum lipid levels. (Table 3)

**Table 3:** Serum Lipid levels and maternal mortality.

Age (yrs)	Case IV	Case III	Case II	Case I
Parity	24	20	22	27
Gestational age (wks)	1	1	1	2
Diagnosis	36	34	38	28
Cholesterol	Sickle cell anemia with severe PIH with HELLP with DIC	Eclampsia with cerebral haemorrhage	Eclampsia with HEELP with DIC with atonic PPH	Severe PE with cerebral haemorrhage

Triglycerides	↑	↑	↑	↑
HDL	↑	↑	↑	↑
LDL	↓	Normal	↓	↓
VLDL	↑	↑	↑	↑
Cause of Death	↑	↑	↑	↑
Age (yrs)	Sickle cell anemia with HELLP with DIC	Eclampsia with cerebral hemorrhage	HELLP with PPH with DIC	Cerebral Haemorrhage

### Discussion

In spite of being a common entity, known since ages, with dangerous implications for the mother and the baby, hypertensive disorders of pregnancy still remain an unsolved problem. They affect pregnancy in many ways, but not all pregnancies are affected in the same way or to similar extent and research continues.

In the present study it was found that there was significant relationship between lipid derangements and severity of hypertensive disorders and its impact on severity of morbidity it causes. Among 964 hypertensive women, the most pathological, serum triglycerides were elevated in 890 (92.32%) women. Other lipids deranged were elevated cholesterol in 637 (66.07%) % women, 453 (46.99%) women had elevated VLDL, 181 (18.77%) women had elevated LDL and 99 (10.26%) women had low serum HDL levels. Among all the lipids, LDL correlated best with the risk of complications, placental abruption, PPH, HELLP, partial HELLP, renal failure and pulmonary edema and more research needs to be done.

In one of our earlier studies Chhabra et al. [15], presence of HELLP/partial HELLP was found to be associated with the adverse pregnancy even in cases of mild hypertensive disorders also as reported by some other researchers Ray et al. [16], Ekhatior and Ebomoyi [17], Vigil-De Gracia P [18] This suggests that something else is also responsible in the pathogenesis of complications in hypertensive disorders during pregnancy. It has been reported that the lipids are deranged in all these subjects Ray et al. [16], Ekhatior and Ebomoyi [19]. All women who died had severe hypertensive disorders and elevated cholesterol, triglycerides, LDL, VLDL levels while, and 3 had below normal HDL levels.

Mudd et al. [19] have reported that high TG, LDL and Cholesterol are modestly associated with the risk of hypertensive disorders of pregnancy and maternal and fetal/neonatal complications. Scifres et al. [20] found that maternal serum fatty acid binding protein 4 (FABP4) levels are elevated before the clinical onset of preeclampsia which was indirect indication of dyslipidemia having a causative relationship with hypertensive disorders of pregnancy and its complications. Ghio et al. [21] have suggested that increased TG during pregnancy appear to increase risk of preeclampsia and preterm birth. Authors suggested that maternal hypertriglyceridemia had a role in

increasing cardiovascular risk later in life and increasing future morbidity. So may be women who have lipid derangements and hypertensive disorders have more chances of cardiovascular disease [22-28].

### Conclusion

As observed dyslipidemia and severity of hypertensive disorders of pregnancy and complications are closely associated. Further research is needed to uncover these associations.

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