

EVALUATION OF BIOCHEMICAL PARAMETERS IN HELLP SYNDROME CASES OF PREGNANCY INDUCED HYPERTENSION AND ECLAMPSIA

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ABSTRACT: Pre-eclampsia is a relatively common complication of pregnancy. HELLP Syndrome (Haemolysis, Elevated Liver Enzymes, Low Platelet) is a pregnancy specific disorder, frequently associated with severe manifestation of Pre-eclampsia and eclampsia with significant morbidity and mortality for pregnant women and their children, but can also be diagnosed in the absence of these disorders. In the present study, the incidence of HELLP Syndrome is 15%. MMR is 11.11% due to DIC, Foetal Morbidity is 44.44%. HELLP Syndrome is more in primigravida, low socio economic groups and AST, ALT, Bilirubin are increased due to Liver Dysfunction.

KEYWORDS: HELLP – Haemolysis, Elevated Liver Enzymes, Low Platelet, DIC - Disseminated Intravascular Coagulation, ARDS - Acute Respiratory Distress Syndrome, AST - Aspartate Transferase, ALT – Alanine Transferase, MMR - Maternal Mortality Rate.

INTRODUCTION: HELLP Syndrome is a multi-systemic disorder. The most widely accepted hypotheses are - a change in the immune Feto maternal balance, platelet aggregation, endothelial dysfunction, arterial hypertension and all inborn error of the fatty acid oxidative metabolism. Hepatic involvement occurs by intravascular fibrin deposition and hypo-volaemia. The recognition of HELLP Syndrome by laboratory tests and the rapid initiation of therapy are required for the improvement of materno-fetal progress.

Pregnancy induced Hypertension is categorized into 3 groups:

1. Hypertension alone,
2. Pre-eclampsia – a mild and severe with proteinuria and pathological oedema and
3. Eclampsia protenuria – pathological oedema along with convulsions.^[1]

HELLP Syndrome is a multi-systemic disorder that complicates pregnancy and has a poor prognosis. It was first described by WEINSTEIN in 1982;^[2,3] the name of the Syndrome (HELL+ HELP) suggests the severity of maternal and fetal prognosis. The acronym is for Haemolysis (H), Elevated Liver Enzymes (EL), Thrombocytopenia (low platelet count - LP). HELLP Syndrome is frequently associated with severe pre-eclampsia and Eclampsia and its incidence is reported to be 0.5-0.9% of all pregnancies and in 10-20% of women with severe Pre-eclampsia (Haram et. al 2009).^[4] Micro-angiopathic hemolytic anemia is the hallmark of the triad. The levels of AST and ALT signifies liver cell Ischaemia or Necrosis and low platelet count less than 100 000 per cubic mm (<100 000 / mm³), is the laboratory criteria for the diagnosis.^[2,3,5, 6,]

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AIM OF THE STUDY: The present study comprises the assessment and evaluation of CLINICAL and BIOCHEMICAL parameters in HELLP Syndrome. Cases of pregnancy induced Hypertension i.e. mild pre-eclampsia, severe pre-eclampsia and eclampsia.

The present study comprises information pertaining to (A) General parameters like age, parity, social-economic status, occupation of the patients, (B) clinical aspects like period of gestation, maternal complications, maternal mortality and foetal outcome, (C) Laboratory Data – Liver enzymes (AST, ALT), Bilirubin, platelet count, Hemolysis. Bleeding time, clotting time, serum uric acid, blood sugar, creatinine, proteinuria, urine for sugar. Thus the aim of the present study is to understand and delineate the importance of above mentioned factors over the incidence and occurrence of HELLP Syndrome in mild pre-eclampsia, severe pre-eclampsia, and Eclampsia.

MATERIALS AND METHODS:

Source: The present study selected out-patients (OP), and patients admitted in the obstetrics and gynaecology wards of King George Hospital, Visakhapatnam. 40 cases of mild pre-eclampsia, 50 cases of Severe Pre-eclampsia (in which 2 cases of HELLP Syndrome), 10 cases of Eclampsia (in which 7 cases are HELLP Syndrome) and 40 cases of normal pregnant women as controls are taken into study. Age, parity, social-economic status, occupation, symptoms and signs of the patients were noted. The Normotensive pregnant women (control) and pregnant women with mild to severe Hypertension were investigated between 20 weeks to 40 weeks of gestation.

Excluded Cases:

1. Haemolytic Uremic Syndrome
2. Idiopathic Thrombocytopenia
3. Viral Hepatitis
4. Acute Fatty Liver of Pregnancy

These cases are excluded from this study.

Sample collection: Random blood samples were taken in sterile container without the addition of anticoagulants, from the out-patients and in-patients under aseptic precautions, and special care was taken to prevent haemolysis. Blood treated with EDTA was used for estimating platelets counts and peripheral smear examination was done for evidence of haemolysis under guidance of clinical pathologist, urine collected in sterile container, tested for albumin and sugar. Tests are done on the same day of sample collection.

Methods: Thorough clinical examination was done along with biochemical investigations. Following were the investigations done:

1. Estimation of Alanine Amino transferase, (Reitman & Frankel 1957)^[7,8]
2. Estimation of Aspartate Amino transferase, (Reitman & Frankel 1957)^[7,8] (Indian Journal, Clinical Pathology 28: 56).
3. Estimation of Total Serum Bilirubin, (Malloy & Evelyn Method 1937)^[7,9]
4. Estimation of Serum Uric acid, (URICASE-POD method).

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5. Estimation of Serum Creatinine, (JAFÉ's method, 1945).
6. Estimation of blood sugar – Glucose oxidase Peroxidase method, (GOD-POD method).
7. Estimation of platelets (count).
8. Peripheral smear for Haemolysis, (Leishman method).^[10]
9. Bleeding time (DUKE's method) and clotting time – capillary tube method of WRIGHT,
10. Urine: Albumin (by Heat coagulation test) and sugar (by Benedict's Reagent).

DISCUSSION: HELLP Syndrome, is a serious variant of pre-eclampsia has been observed in 10% of pregnancies approximately by various study groups associated with life threatening complications like DIC, pulmonary oedema, cerebral thrombosis, Renal failure, Hepatic haematomas and rupture, ARDS, Ascites, puerperal sepsis and a variety of Hemorrhagic complications are studied by various research groups.^[11]

The study consists of 40 cases of mild pre-eclampsia, 50 cases of Severe Pre-eclampsia (in which 2 cases of HELLP Syndrome), 10 cases of Eclampsia (in which 7 cases are HELLP Syndrome) and 40 cases of normal pregnant women as controls. 9 cases of HELLP Syndrome are detected in total 60 cases of severe pre-eclampsia & eclampsia.

Clinical and Biochemical profile are analysed under the following categories: (i) Mild Pre-eclampsia, (ii) Severe Pre-eclampsia and (iii) Eclampsia. (HELLP Syndrome).

The results pertaining to this category are analysed as per (A) General parameters like age, parity, incidence, social-economic status, occupation (Table 1), (B) Clinical parameters like period of gestation, maternal complications and Foetal outcome (Table 1), and (C) Laboratory Data (Table 2 (i), 2 (ii), 2 (iii), 2 (vi)) of symptoms and signs of the patients were noted.

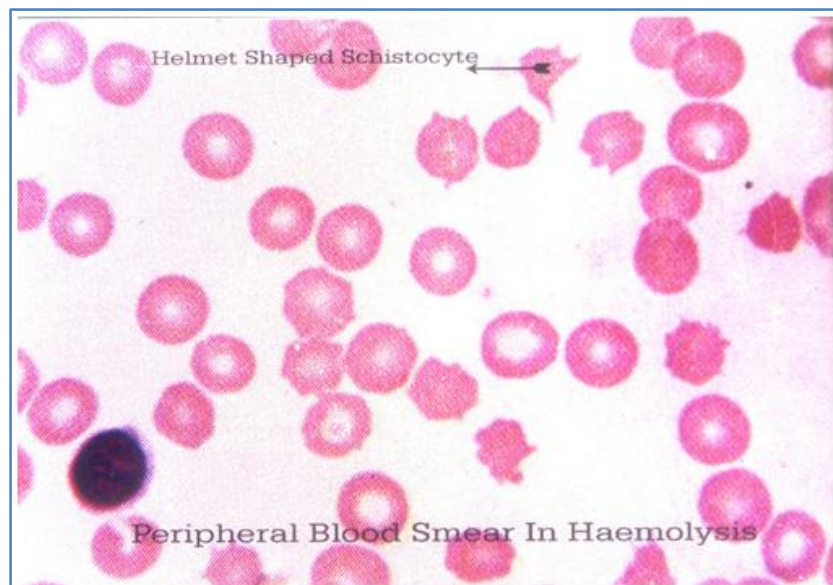


Fig. 1: Helmet shaped Cells Schistocytes

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Parameter	Controls (40 Cases)	Mild Pre eclampsia (40 cases)	Severe Pre eclampsia (50 cases)	Total(Severe Pre eclampsia and Eclampsia) (60 cases)
Incidence:	No HELLP cases	No HELLP cases	2 HELLP cases and without HELLP cases: 48	9 HELLP cases (2+7)
Parity	P - 30(75%) M - 10(25%)	P - 32(80%) M - 8(20%)	P - 40(83%) M - 8(17%)	P - 6(67%) M - 3(33%)
Socio economic:				
Group I (income < Rs. 6000/month)	15(38%)	25(62%)	40(83%)	8(89%)
Group II (income > Rs.6000/month)	25(62%)	15(38%)	8(17%)	1(11%)
Occupation:	Home makers: 38(95%) Wage earners: 2(5%)	Home makers: 36(90%) Wage earners: 4(10%)	Home makers: 43(90%) Wage earners: 5(10%)	Home makers: 8(89%) Wage earners: 1(11%)
Gestational age(mean) :	35 weeks(±2days)	37 weeks(±2days)	36 weeks	34 weeks (±6days)
Maternal complications:	nil	Nil	nil	100% (Mortality: 11%)
Foetal Mortality:	2.56%	2.56%	16.65%	44.44%

Table 1

In the 9 HELLP Syndrome cases, Maternal complications are 3 cases of Abruuptio Placenta, 1 case of DIC, 1 case of Ascites, 1 case of cerebral thrombosis (Hemiplegia), 2 cases of jaundice and 1 case of puerperal sepsis.

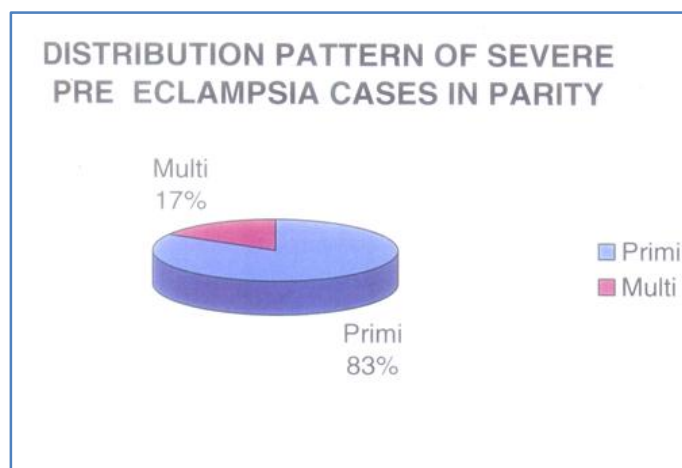


Fig. 2: Distribution pattern of Severe Pre eclampsia cases in parity

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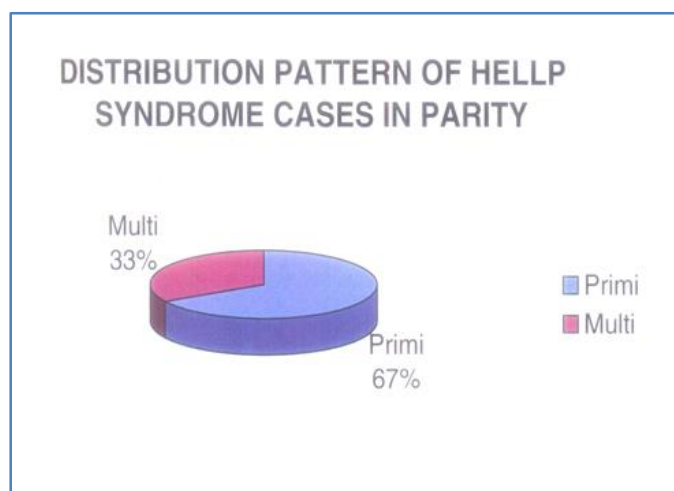


Fig. 3: Distribution pattern of HELLP Syndrome cases in parity

Group	AST (SGOT) u/l				ALT (SGPT) u/l			
	Mean	SD	SEM	P Value	Mean	SD	SEM	P Value
Controls	28.78	20.6	3.26	0.0158	19.95	5.23	0.83	<0.01
Mild Pre eclampsia	31.10	11.4	1.81	0.2071	40.38	20.30	3.21	<0.001
Severe Pre eclampsia	88.72	29.5	4.18	<0.001	96.35	42.0	5.88	<0.001
HELLP Syndrome eclampsia	524.06	144.98	48.33	<0.0001 (more significant)	376.14	137.71	45.90	<0.0001 (more significant)

Table 2 (i): Laboratory Data

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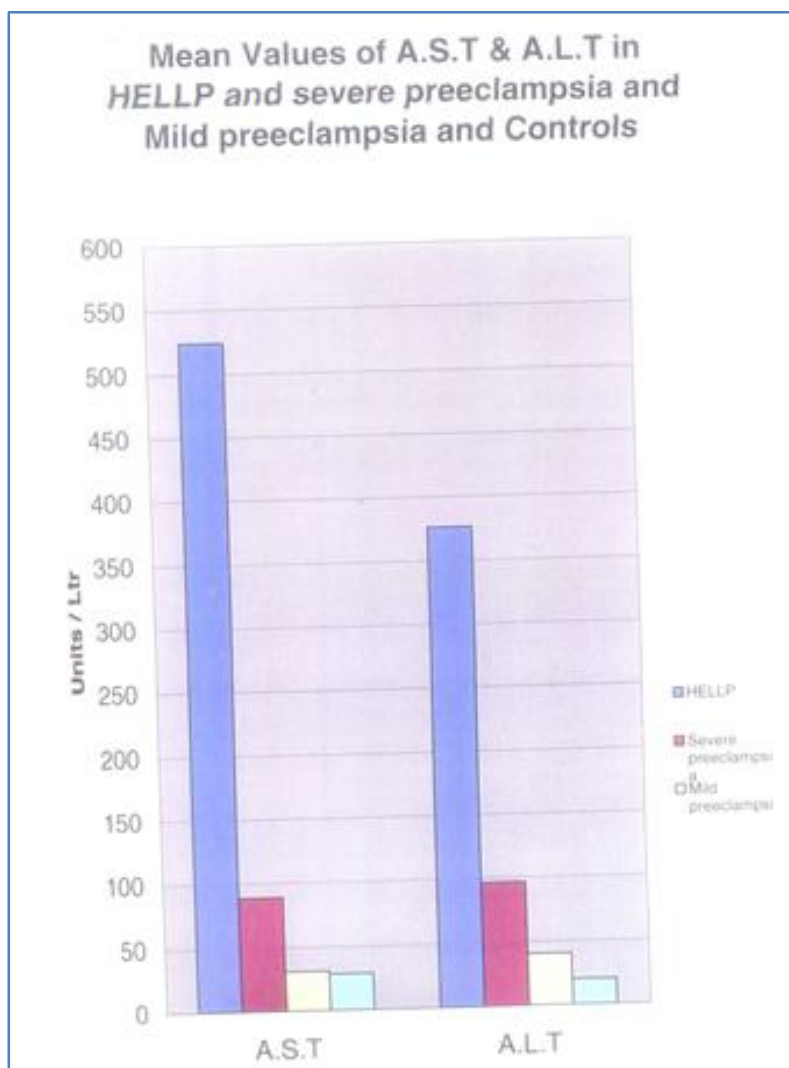


Fig. 4: Mean values of AST & ALT in HELLP Syndrome eclampsia, Severe Pre eclampsia, Mild Pre eclampsia and Control cases

Group	Bilirubin (in mg/dl)				Platelet (in lakh /m m ³)			
	Mean	SD	SEM	P Value	Mean	SD	SEM	P Value
Controls	0.58	0.12	0.02	0.0265	2.74	0.41	0.07	0.0177
Mild Pre eclampsia	0.61	0.11	0.02	0.0938	2.71	0.36	0.06	0.6360
Severe Pre eclampsia	0.64	0.10	0.01	0.0089	2.38	0.51	0.07	0.001
HELLP Syndrome eclampsia	1.71	0.99	0.33	<0.0001 (more significant)	0.93	0.99	3.29	<0.0001 (more significant)

Table 2 (ii): Laboratory Data

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Group	Uric acid (in mg/dl)				Creatinine (in mg /dl)			
	Mean	SD	SEM	P Value	Mean	SD	SEM	P Value
Controls	3.13	0.70	0.11	0.0243	0.67	0.21	0.03	0.0173
Mild Pre eclampsia	4.28	1.4	0.23	0.0001	0.66	0.14	0.02	0.7685
Severe Pre eclampsia	6.23	1.33	0.20	0.0001	0.85	0.20	0.03	0.0001
HELLP Syndrome eclampsia	8.72	0.48	0.16	<0.0001 (more significant)	1.30	0.10	0.03	0.0001 (more significant)

Table 2 (iii): Laboratory Data

Group	BT Mean	CT Mean	Proteinuria	Haemolysis
Controls	2 min 8 sec	4 min 50 sec	Absent	Absent
Mild Pre eclampsia	2 min 8 sec	4 min 5 sec	47.50%	Absent
Severe Pre eclampsia	2 min 8 sec	4 min 5 sec	100%	Absent
HELLP Syndrome	3 min 10 sec (1 case 8 min 30 sec)	8 min 41 sec (1 case 11 min 9 sec)	100%	Burr cello & HELMET shaped Schistocytes present (fig 1)

Table 2 (iv): Laboratory Data

In the present study, the incidence of HELLP Syndrome is 15%, MMR is also 11.11% due to DIC. Foetal Mortality is 44.44%. The incidence of HELLP Syndrome is more in Primigravida, between 20-30 years in low socio economic groups at 34 weeks \pm 6 days of period of gestation (Table 1). Depend upon the platelet count Martin et al.^[12]

At University of Mississippi have further categorized the HELLP Syndrome into 3 classes.

Class I: Platelet counts < 50 000 / mm³

Class II: Platelet counts > 50 000 to < 100 000 / mm³

Class III: Platelet counts > 100 000 / mm³

If platelet count is < 100 000 / mm³, it is ominous sign to terminate the pregnancy. In HELLP Syndrome marked elevation of Liver Enzymes present, P value for AST, ALT, Bilirubin, Platelet, Uric Acid and Creatinine are highly significant (P value < 0.0001), compared with controls & Mild Pre eclampsia & Severe Pre eclampsia and also with previous studies.

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Study	AST u/l Mean ±	ALT u/l Mean ±	Bilirubin mg/dl Mean ±	Platelet Lakhs/mm ³ Mean ±	Uric acid mg/dl	Creatinine mg/dl Mean ±
M.SIBAI.MARK TASLIM, AJ OBG (1986) (pp.155- 501) ^[13]	434±55.6	-	2.7±2.5	55±23	8.3±3.1	1.71±2.0
Magann Everttf Kenneth, OBG (1994) (pp.171- 1154-1158) ^[14]	197±232	158.2±16.4	-	99.1±67.9	7.2±1.8	-
Alfredo Nova MD Boaha, (1991) (pp.165-724- 727) ^[15]	280±86 (P value 0.001)	-	-	44±70 (P value < 0.001)	7.35±0.41	-
Present Study	524±48.33	376±45.90	1.71±0.33	93±3.29	8.72±0.16	1.30±0.03

Table 3

Among 9 cases of HELLP Syndrome, 8 cases had normal BT and CT and clot retraction time. In one case BT (8 min 30 sec), CT (11 min 9 sec) prolonged & clot retraction time is prolonged & there was abruption placenta. This case died due to post partum hemorrhage, secondary to DIC. In this case AST 689.65 u/l, ALT 379.31 u/l, platelet count 80 000 / mm³, Bilirubin 3.3mg/dl, BT 8 min 30 sec, CT 11 min 9 sec, clot retraction time 30 minutes, uric acid 8.2 mg /dl, serum creatinine 1.4 mg/dl, urine albumin.⁺⁺⁺

In Louis Weinstein study,^[2,3] Hematological parameters consisting of BT, CT & Prothrombin time were reported to be normal in 96%. In present study the findings are similar to that of Weinstein et al. Liver dysfunction in these cases causes compositional changes in the RBC membrane due to plasma lipids interchange producing echinocytes.^[16]

CONCLUSION: The Biochemical parameters estimated are Liver Enzymes - AST, ALT and Bilirubin and peripheral smear for Haemolysis. These enzymes significantly elevated in HELLP Syndrome. Thrombocytopenia is present. Hence, the severity of metabolic disturbances can be monitored by Liver Enzymes Estimation, Platelet count and peripheral blood smear. The early recognition of HELLP Syndrome and the initiation of early therapy are required in order to ensure the favorable evaluation of the mother and foetus.

The incidence of MMR is more in HELLP Syndrome cases, wherein, if platelet count is <100,000 / mm³ - it is ominous sign to terminate the pregnancy.

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REFERENCES:

1. Williams, American College of Obstetrician and Gynecologists (1986), 19th ed; 763-64.
2. Weinstein L., Syndrome of hemolysis, elevated liver enzymes, and low platelet count: a severe consequence of hypertension in pregnancy, *Am J Obstet Gynecol.* 1982 Jan 15; 142 (2): 159-67.
3. Weinstein L., Preeclampsia/eclampsia with hemolysis, elevated liver enzymes, and thrombocytopenia, *Obstet Gynecol.* 1985 Nov; 66 (5): 657-60.
4. Haram K, Svendsen E, Abildgaard U (Feb 2009). "The HELLP syndrome: clinical issues and management. A review" (PDF). *BMC Pregnancy Childbirth* 9: 8. doi: 10.1186/1471-2393-9-8.
5. O'Brien J. Buckley, O.Munk PL, Torreggiani WC, An unusual case of elevated Liver Enzymes (2006): 10b, Hepatic necrosis following HELLP Syndrome, *EUR Radio* 1 (2007), 17: 289: 291.
6. Miha D, Costin N, Miha C M, Seicean A, Ciortea R. J. Gastrointestinal Liver disease, Dec. 2007; 164:419-424.
7. Varley H. 'Practical Clinical Biochemistry', Edition 4th Heinemann Medical 1967; 289-297.
8. H. U. BERGMAYER, *Methods of Enzymatic Analysis*, 1974; 3:1-30.
9. Robert K. Murray Harper's 'Illustrated Biochemistry', 28th Edition, McGraw-Hill pp. 241-242.
10. SIBAI BM Diagnosis, controversies and management of the Syndrome of Hemolysis, Elevated Liver Enzymes, Low Platelet count, *Obstetrics and Gynecology* (2004);103:981-991.
11. Menon, Devi, Datta & Biswas, Dutt, Goswami & Dawn, Rao, GUN et al, Safdar Jung Hospital, New Delhi, 1972.
12. Martin JN, Owens MY, Keiser SD, Parrish MR, Tam Tam KB, Brewer JM, Cushman JL, May WL. Standardized Mississippi Protocol treatment of 190 patients with HELLP syndrome: Slowing disease progression and preventing new major maternal morbidity. *Hypertens Pregnancy*, 2012; 31 (1): 79–90.
13. Baha M. Sibai, Mark M. Taslimi, Adel El-Nazer, Erol Amon, Bill C. Mabie, George M. Ryan. Maternal-perinatal outcome associated with the syndrome of hemolysis, elevated liver enzymes, and low platelets in severe preeclampsia-eclampsia. *Am J Obstet Gynecol.*, September, 1986;155(3):501-507.
14. Everett F. Magann; Kenneth G. Perry Jr.; Edward F. Meydrech; Robert L. Harris; Suneet P. Chauhan; James N. Martin Jr. (Profiled Author: Suneet P. Chouhan), Postpartum corticosteroids: Accelerated recovery from the syndrome of hemolysis, elevated liver enzymes, and low platelets (HELLP) , *Am J Obstet Gynecol.*, 1994;171(4):1154-1158.
15. Alfredo Nova, Baha M. Sibai, John R. Barton, Brian M. Mercer, Murray D. Mitchell, Maternal plasma level of endothelin is increased in preeclampsia, *Am J Obstet Gynecol.*, September 1991;165(3):724–727.
16. Rahman TM, Wendon J, Severe Hepatic Dysfunction in pregnancy, *QJM* (2002), pp.95, 343-35.

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