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PREVALANCE OF HELLP SYNDROME IN PREECLAMPSIA AND ITS FETOMATERNAL OUTCOME IN JHARKHAND INDIA

Gynaecology

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ABSTRACT

INTRODUCTION: Preeclampsia being a serious challenge in tropical obstetrics. It seriously affects hematological and biochemical changes in body named as HELLP SYNDROM leading to poor feto-maternal outcome.

AIM: Prospective interventional study aimed at determining the prevalence of HELLP SYNDROME with respect to COMPLETE AND PARTIAL HELLP SYNDROME in preeclampsia and its fetomaternal outcome.

METHOD: One year of prospective study from June 2016 to May 2017 done on patient attending emergency labour room in RIMS, Ranchi, Jharkhand INDIA. 100 Patient with preeclampsia was selected and hematological and biochemical study (CBC, Platelet count, BT, CT, LFT , Sr. LDH, RFT, URIC ACID,PT-INR) was done to know whether patient suffering from HELLP SYNDROME . Maternal outcome studied in terms of maternal age, parity, mode of delivery ,its complication and outcome . Fetal outcome studied with respect to its prematurity, IUGR, IUD, APGAR score.Fisher's exact test was used for inferential analysis to search for associations among preeclampsia and HELLP Syndrome and its fetomaternal outcome.

RESULTS: Study done on 100 preeclamptic patients, 4% complete HELLP syndrome, 14% partial HELLP syndrome. 25% of cases among HELLP syndrome were booked. All patients were elders. 50% of the patient with complete HELLP syndrome were multigravida and 50% were primigravida. Similarly 40% of the patient with partial HELLP syndrome were multigravida and 60% were primigravida. Onset was antepartum in 90% and 10% it was postpartum. Maternal outcome is caesarean section in 40%: uncontrolled hypertension (20%), meconium stain liquor (10%) and fetal distress (5%). In 5% subtotal hysterectomy done because of uncontrolled postpartum haemorrhage, 20% required platelet transfusion. Perinatal outcome was 45% preterm labour, 28% intrauterine death, 67% NICU admission.

CONCLUSION : Preeclampsia with severe features and eclampsia is common among the adolescents, unbooked, rural, and low socio-economic group of women in this study.There is need for policy makers to formulate policies toward female education, awareness for ANC check up and provision of social amenities in rural areas.

KEYWORDS

HELLP SYNDROME, preeclampsia ,hysterectomy,prematurity, IUGR, IUD, APGAR score.

INTRODUCTION:

Preeclampsia being a serious challenge in tropical obstetrics. It seriously affects hematological and biochemical changes in body named as HELLP SYNDROM leading to poor feto-maternal outcome. Obstetrics is a continually changing subject where new diseases are being identified ,old diseases defined ,new etiologies discovered and new treatment modalities being evolved . Hypertension is one of the commonest complications during pregnancy through out the world. Preeclampsia is a multisystem disorder of vascular function , specific to pregnancy ,which is typically characterized by hypertension , proteinuria , edema and fetal compromise . It arises in the placenta , probably as a result of ischemia and propagates through the maternal vascular tree such that all the organ systems are affected . It has consistently been one of the top causes of maternal mortality in the UK since the start of the confidential enquiry into the maternal mortality in 1952 and is now one of the common obstetric associations of perinatal death [1]. Treatment of this disorder remains a challenge to even the most experienced obstetricians mainly because the exact etiology is unknown. Consequently management is directed towards detection of the disorder at an early stage and to effect or atleast ameliorate it's progression in an attempt to achieve fetal maturity while preventing maternal complications. Judicious prophylactic administration of magnesium sulphate and timely termination of pregnancy may improve fetal salvage without putting the mother at high risk. Preeclampsia is the major cause maternal and perinatal mortality and morbidity worldwide causing 15% of all direct maternal death in the UK and 24% of all the maternal deaths in India .[2] There is 5 fold increase in perinatal mortality in preeclampsia with iatrogenic prematurity being the common culprit [3]. Eclampsia is a more significant cause of perinatal mortality and morbidity in the non industrialized countries (up to 40 % of perinatal deaths) [4].

Cases that were variants of severe preeclampsia – eclampsia with atypical signs and symptoms or very complicated course of this disease process have been reported since the end of the 19th century . Many of these description of pregnancies complicated by an uncharacteristic presentation of preeclampsia are representative of the condition now identified as HELLP syndrome. A syndrome characterized by haemolysis, elevated liver enzymes, and low platelet count syndrome was first described by Pritehard et al. in 1954[5]. HELLP syndrome develops in 1 of 1000 pregnancies overall, and in 4 – 12% of the patients already affected by severe preeclampsia or eclampsia. Presentation largely depends on the stage of the disease. Approximately 90% of the patients present with generalized malaise suggestive of a viral illness[8]. Because early diagnosis of HELLP is critical, pregnant woman who present with symptoms such as malaise in the second half of their pregnancy should be immediately evaluated with complete blood count and liver function tests to exclude it. Other common symptoms include epigastric or right upper quadrant abdominal pain, nausea, vomiting, headache and visual symptoms. At times, referred pain from the liver can produce atypical neck and shoulder pain. Any pregnant patient with epigastric or right upper quadrant abdominal pain in the second half of pregnancy, particularly if in association with nausea and or vomiting, has HELLP syndrome until proven otherwise. When the upper abdominal pain is writhing in nature and of sudden onset, hepatic bleeding or rupture is the likely cause, constituting an obstetric emergency. A small subset of patients may present with symptoms related to their thrombocytopenia, such as mucosal bleeding, petechial hemorrhages, ecchymosis or hematuria. Thus this study was design to studyprevalance of HELLP syndrom in preeclampsia and its fetomaternal outcome.

MATERIALS AND METHODS :

One year of prospective interventional study from June 2016 to May 2017 done on patient attending emergency labour room in RIMS, Ranchi, Jharkhand INDIA. Out of which 100 Patient with preeclampsia was selected randomly and biochemical and heamatological investigations given.

INCLUSION CRITERIA :

1. When blood pressure was 140/90 mm of Hg or more after 20

weeks of period of gestation.
2. When there was associated proteuriaof 300 mg/24 hrs.
3. Any subjective C/O headache, blurred vision, malaise, nausea, vomiting, persistent epigastricpain, scanty urination, seizure super imposed on BP of 140/90 mm of Hg or more.
4. Any patient presenting with features suggestive of IUGR, oligohydramnios with the rise of the blood pressure were also be included.

EXCLUSION CRITERIA:
1. Known heart disease leading to hypertension.
2. Known renal disease.
3. Previous history of jaundice or liver disease.
4. Coartation of aorta, pheochromocytoma, systematic lupus erythromatosus.
5. Subjects not willing to undergo the study.

STUDY TOOLS AND TECHNIQUES

Patients attending antenatal clinic and admitted in labour room through emergency screen as per propharma. Approval of ethical committee was taken and subjects were enrolled after adequate inform consent.

They will be subjected to detailed history, clinical examination and appropriate investigations. Every individual will be allocated into one of the following groups:-
1) Pregnant mothers complicated with preeclampsia having the features of HELLP syndrome.
2) Mothers with preeclampsia in addition to partial HELLP syndrome.
3) Mothers with preeclampsia without the laboratory features of HELLP syndrome.

The patients will be followed till delivery and consequent fetal and maternal outcome will be revealed.

Socio economic status, Chief complaints, History of present illness(First trimester,Second trimester, Third trimester) Obstetric history (Gravida , Parity), Past medical history, Family history, Personal history ,Drug history ,Physical examination, (General survey, Consciousness, Weight ,Any abnormal weight gain , Pallor ,Edema, Pulse, B P, Jaundice ,Thyroid, Heart, Lung)

Obstretric examination (Per abdomen, Any scar mark, Symphysio fundal height ,Abdominal girth, Lie, Presentation, Liquor volume, Fetal movement, Fetal heart sound)

INVESTIGATIONS
1. Serial measurement of blood pressure after 20 weeks of gestational age.
2. Serial measurement of body weight.
3. Haemoglobin percentage.
4. Haematocrit
5. Reticulocyte count.
6. Peripheral blood smear.
7. Platelet count
8. Urea, Creatinine.
a. Uric acid
9. Urinary total protein
10. Total bilirubin
11. Liver enzymes -- aspartate amino transferase and alamine amino transferase.
12. Lactate dehydrogenase.
13. Sonographic evaluation of feto placental profile.
14. Birth weight
15. Gestational age (term / preterm).
16. APGAR score
17. Admission in neonatal intensive care unit.

Intrapartumcare: (Progress of labour, Change in blood pressure, Complication, Mode of delivery, Post-partum blood pressure) Placenta (Retro placental clot)

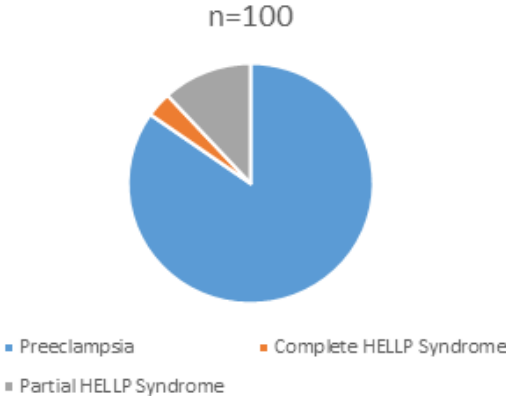
Fetal outcome :(Live / still born, Apgar score at 1 min, Birth weight, Maturity, Resuscitation, Admission in NICU)

All data were processed based on the instruments standards. Socio-demographic data were analyzed descriptively in terms of means and standard deviations. Fisher's exact test was used for inferential analysis to search for associations among preeclampsia and HELLP Syndrom and its fetomaternal outcome.

RESULTS:

TABLE 1 - PREVALENCE

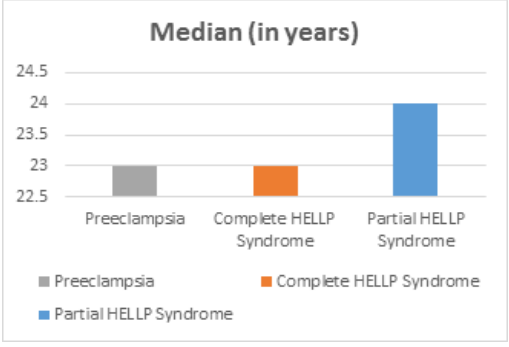
PREVALENCE	n=100
HELLP syndrome	18 (18%)
Complete HELLP syndrome	4 (4%)
Partial HELLP syndrome	14 (14%)



Study prevalence of HELLP SYNDROME in mothers with preeclampsia is 18 % . Features of complete HELLP in 4 cases and remaining 14 patients with partial HELLP SYNDROME

TABLE 2 - DISTRIBUTION OF AGE

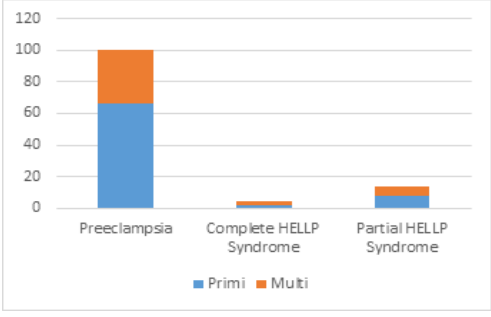
Age (in yrs)	Mean + SD
Preeclampsia	23 + 5
HELLP syndrome	23 + 4
Partial HELLP syndrome	24 + 5



Study reveals age HELLP SYNDROME: 25 ± 4 yrs.The value in cases of complete HELLP SYNDROME was 23 years .Preeclampsia was 23 years. The standard deviation of age in HELLP SYNDROME and preeclampsia were 4 and 5 respectively

TABLE 3 - DISTRIBUTION OF PARITY

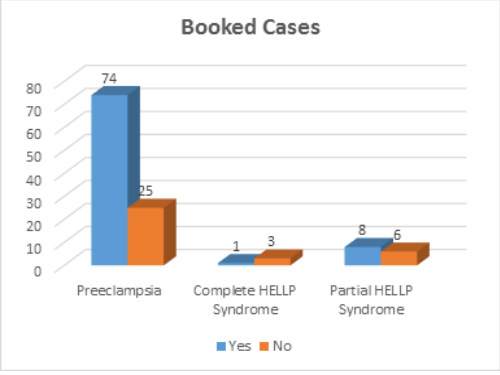
Preeclampsia n= 100	66 (66%)	34 (34%)
HELLP syndrome n=4	2 (50 %)	2 (50%)
Partial HELLP syndrome (n = 14)	8 (54 %)	6 (46 %)



The corresponding figures of primigravida in patients with Complete HELLP SYNDROME, partial HELLP SYNDROME and preeclampsia were 50%, 54 % and 66 % respectively

TABLE 4 - BOOKED CASES

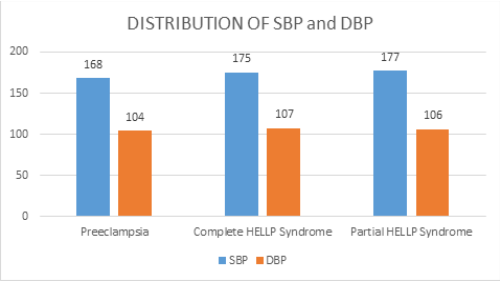
Booked cases	Yes	No
Preeclampsia	74 (74%)	25 (25%)
HELLP syndrome	1 (25%)	3 (75%)
Partial HELLP syndrome	8 (57.14%)	6 (42.85%)



This chart also shows that only the 25% of cases among HELLP syndrome were booked

TABLE 5 - DISTRIBUTION OF SBP, DBP, GA ON ADMISSION AND GA AT DELIVERY IN PREECLAMPSIA AND HELLP SYNDROME

	Preeclampsia	Complete HELLP syndrome	
	Mean + SD	Mean + SD	P value
SBP (in mm of Hg)	168 + 14	175 + 15	.02
DBP (in mm of Hg)	104 + 5	107 +7	.02
GA on admission	36 wks 3 d 2 wks 2 d	35 wks + 3 wks	.01
GA at delivery	36 wks 5 d + 2 wks	35 wks 2 wks	.00

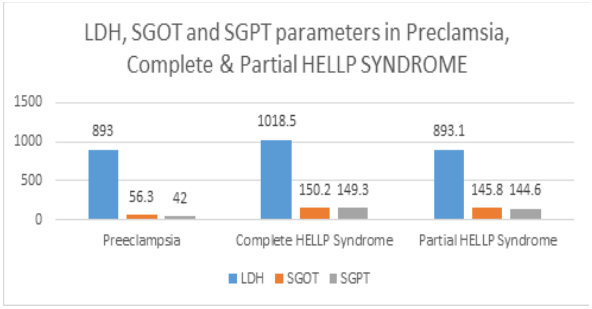


The mean values for SBP of mothers with Complete HELLP SYNDROME and preeclampsia are 175.6 and 168 mm of Hg.

Fisher's exact test 2-tailed p value < 0.02 (between preeclampsia and complete HELLP syndrome)

TABLE 7 - HAEMATOLOGICAL AND BIOCHEMICAL PARAMETERS IN PREECLAMPSIA AND COMPLETE HELLP SYNDROME

	Preeclampsia	Complete HELLP syndrome	
	Mean SD	Mean SD	P value
Hb (gm %)	10.3 1.21	9 1.48	.00006
Platelet count (in cmm)	273449 80021.31	170590 56000	.000
LDH (u/l)	893 ± 359.3	1018.5 ± 383.7	.000
Total bilirubin (mg /dl)	.9 ± .45	2.7 ± 1.61	.000
SGOT(u/l)	56.3 ± 11.03	150.2 ± 72.88	.000
SGPT(u / l)	42 ± 7.53	149.3 ±70.89	.000



Haemolysis in peripheral blood smear was found to be significant in HELLP syndrome (56%) than preeclampsia (12%) and the p value was < .0003 .

The mean values for the lactate dehydrogenase of the Complete HELLP syndrome group and preeclampsia were 1018 and 749.5 U / ml The mean values for total bilirubin of the Complete HELLP syndrome group was 2.7 mg/dl with p value .0003

The mean for SGOT of the patients with Complete HELLP syndrome and preeclampsia were 150.2 U/ml and 56.3 U/ml ; the p value was calculated as .000

TABLE 9 - EVIDENCE OF HAEMOLYSIS BY PERIPHERAL BLOOD SMEAR

PBS	Normal	Haemolysis
Preeclampsia	88 (88%)	12 (12%)
Complete HELLP syndrome	1(31%)	3 (68%)

TABLE 10 - MODE OF DELIVERY IN PREECLAMPSIA AND COMPLETE HELLP SYNDROME

	Preeclampsia (n = 100)	Complete HELLP syndrome (n= 4)	P value
LSCS	38 (38%)	2 (50%)	.423
Emergency	12 (12%)	1 (25 %)	.138
Elective	16 (16%)	0	
VD	62 (62 %)	3 (75 %)	
Spontaneous	28 (28%)	2(50 %)	.029
Induced	34 (34 %)	1(25%)	

50 % and 38 % of patients with HELLP syndrome and preeclampsia undergo CAESAREAN SECTION . Patients with HELLP syndrome undergoing emergency caesarean section were 25 %. After stabilising heamodynamic parameters

VAGINAL ROUTE was the mode of delivery for 50 % with HELLP syndrome. 27.27 % and 8.63 % undergo spontaneous vaginal delivery patients with HELLP syndrome and preeclampsia respectively . Induction done in 25%.

TABLE 11 - ASSOCIATION OF BIRTH WEIGHT AND APGAR SCORE IN PREECLAMPSIA AND COMPLETE HELLP SYNDROME

	Preeclampsia	Complete HELLP syndrome	
	Mean + SD	Mean + SD	P value
BW of the baby (in gm)	2477.5 + 425.33	1913 + 628.86	.000
Apgar score (at 1 min)	5.4 + 2.73	5 + 2.69	.139

TABLE 12 - ASSOCIATION OF BIRTH WEIGHT AND APGAR SCORE IN PREECLAMPSIA AND PARTIAL HELLP SYNDROME

	Preeclampsia	Partial HELLP syndrome	
	Mean + SD	Mean + SD	P value
BW of the baby (in gm)	2477.5 + 425.33	2022.6 + 666.64	.007
Apgar score (at 1 min)	5.4 + 2.73	5.4 + 2.73	.28

BABY WEIGHT: The majority of low birth weight babies in the Complete HELLP syndrome

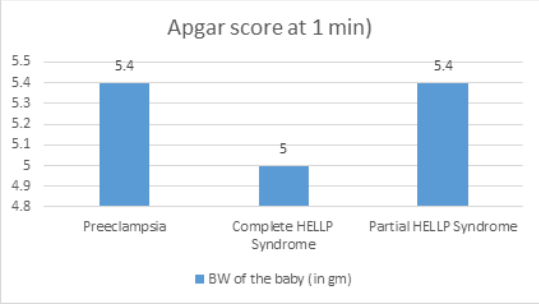


TABLE 13 - PERINATAL OUTCOME IN PREECLAMPSIA AND COMPLETE HELLP SYNDROME

	Preeclampsia n=100	Complete HELLP syndrome n=4	P value
IUD	6 (6%)	2(50%)	.003
IUGR	19 (19 %)	1(25%)	.412
Neonatal death	4 (4 %)	1(25%)	.001
Admission in NICU	26 (26%)	2(50%)	.001

BABY OUTCOME:
The rate of babies admitted in NICU in patients with HELLP syndrome were significantly different from that in preeclampsia group as evident by p value of .001 .The rate of neonatal death in patients with HELLP syndrome and preeclampsia were significantly different as the p value was .01

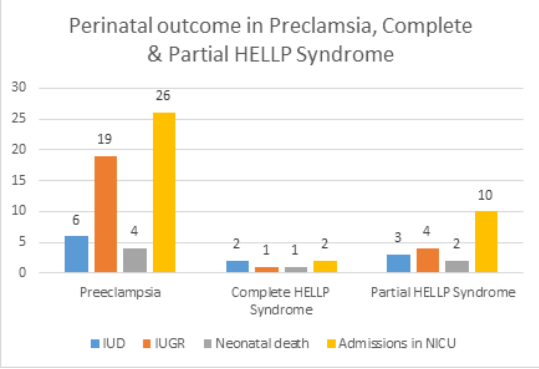
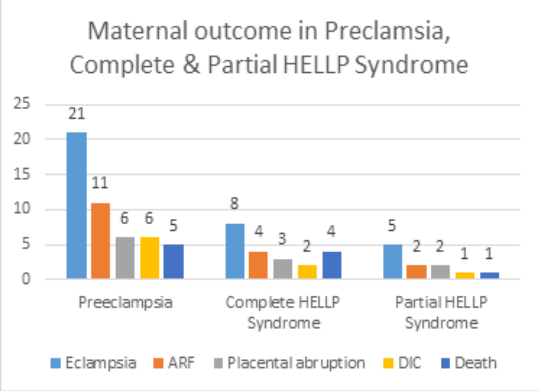


TABLE 14 - MATERNAL OUTCOME IN PREECLAMPSIA, HELLP SYNDROME AND PARTIAL HELLP SYNDROME

Complications	Eclampsia	ARF	Placental abruption	DIC	Death
Preeclampsia	21 (7.55%)	11 (3.96%)	6 (2.15%)	6 (2.15%)	5 (1.79%)
HELLP syndrome	8 (36.36%)	4 (18.18%)	3 (13.63%)	2 (9.09%)	4 (18.18%)
Partial HELLP syndrome	5 (31.25%)	2 (12.5%)	2 (12.5%)	1 (6.25%)	1 (6.25%)



MATERNAL OUTCOME:
ECLAMPSIA occurred in 36.36% and 7.55% in patients with HELLP syndrome and preeclampsia respectively.

18.18% and 3.96% of patients with HELLP syndrome and preeclampsia had ACUTE RENAL FAILURE .

13.63% and 2.15% of patients with HELLP syndrome and preeclampsia suffered from DISSEMINATED INTRAVASCULAR COAGULATION .

PLACENTAL ABRUPTION had been found in 9.09%, 6.25% and 2.15% of patients with HELLP syndrome ,partial HELLP syndrome and preeclampsia .

MULTIORGAN DYSFUNCTION was an important complication in 9.09% , 6.25% and 3.59% of mothers with HELLP syndrome ,partial HELLP syndrome and preeclampsia respectively.

MATERNAL MORTALITY was found in 18.18%, 6.25 % and 1.79 % of cases with HELLP syndrome, partial HELLP syndrome and preeclampsia.

DISSCUSSION:
Study prevalence of HELLP SYNDROME in mothers with preeclampsia is 18 % . Features of complete HELLP in 4 cases and remaining 14 patients with partial HELLP SYNDROME

American Academy of Physicians[7] found that 4% to 12% of patients with severe preeclampsia or eclampsia develop signs of HELLP SYNDROME

The reasons for this discrepancy may be the lack of uniformity among the results of different studies

PARITY: Most of the patients in all the three groups are primigravida The corresponding figures of primigravida in patients with Complete HELLP SYNDROME, partial HELLP SYNDROME and preeclampsia were 50%, 54 % and 66 % respectively.

Chabra et al [8]described 615 rural Indian women with PIH and opined that 1.5 % of primigravida and 1.2% of multigravida had complete HELLP syndrome ; 26.5% of primi and 13.85% of multigravida patients with PIH had partial HELLP syndrome and 44.6% of patients without HELLP syndrome

The study done by Padon[9]revealed that, in contrast to preeclampsia, HELLP syndrome is more often associated with Caucasian multiparous women

The discordance in finding noted in the present study from other studies could be probably due to different racial factors.

AGE: Study reveals age HELLP SYNDROME: 25 ± 4 yrs.

The value in cases of complete HELLP SYNDROME was 23 years Preeclampsia was 23 years

The standard deviation of age in HELLP SYNDROME and preeclampsia were 4 and 5 respectively no significant difference between the two variables with p value .92.

American Academy of Physicians[7]- less than 25 years old Joelcio Fransisco Abbade[10]et al - within 19 to 34 years old range)

Different studies show different statistics, the possible reason being the difference in the geographical pattern and different ethnicity

BOOKED: 75% were unbooked cases with HELLP SYNDROME

Majority of cases with HELLP SYNDROME referred from outside. Our study corroborates with the finding of Ching Ming Liu[11] et al. showing majority of cases with HELLP syndrome referred from outside.

Study shows majority 0f patients came from interior, illiterate and unaware about health check-up, it may be cause of majority of unbooked cases

Different studies show different statistics, the possible reason being

BLOOD PRESSURE:
The mean values for SBP of mothers with Complete HELLP SYNDROME and preeclampsia are 175.6 and 168 mm of Hg.

The disease process which may be present even when blood pressure is

not grossly elevated (American Academy of Family Physicians[7])

(SatpathiHemant K[11] et al 25 reported that as many as 15 - 20% of patients with Complete HELLP SYNDROME do not have antecedent hypertension. Diagnosis is notoriously difficult in those patients)

PERIPHERAL BLOOD SMEAR:
Haemolysis in peripheral blood smear was found to be significant in HELLP syndrome (56%) than preeclampsia (12%) and the p value was < .0003 .

The mean values for the lactate dehydrogenase of the Complete HELLP syndrome group and preeclampsia were 1018 and 749.5 U / ml The mean values for total bilirubin of the Complete HELLP syndrome group was 2.7 mg/dl with p value .0003

The mean for SGOT of the patients with Complete HELLP syndrome and preeclampsia were 150.2 U/ml and 56.3 U/ml ; the p value was calculated as .000

MODE OF DELIVERY:
50 % and 38 % of patients with HELLP syndrome and preeclampsia undergo CAESAREAN SECTION . Patients with HELLP syndrome undergoing emergency caesarean section were 25 %. After stabilising heamodynamic parameters

VAGINAL ROUTE was the mode of delivery for 50 % with HELLP syndrome. 27.27 % and 8.63 % undergo spontaneous vaginal delivery patients with HELLP syndrome and preeclampsia respectively . Induction done in 25%.Though our study shows variation, yet the values differ as different studies do not show any uniform result, it depend on different institution, situation of patient and decision of consultant

BABY WEIGHT:
The majority of low birth weight babies in the Complete HELLP syndrome

BABY OUTCOME:
The rate of babies admitted in NICU in patients with HELLP syndrome were significantly different from that in preeclampsia group as evident by p value of .001

The rate of neonatal death in patients with HELLP syndrome and preeclampsia were significantly different as the p value was .01

APGAR SCORE:
The mean values for the apgar score at one minute for the patients with Complete HELLP patients and preeclampsia were 5 and 5.4 respectively but surprisingly the values do not show any significant difference as the p value was .139.which is similar to Ching Ming liu[13] et al.

PERINATAL OUTCOME:intrauterine fetal death was found in 50%, 21.42 % and 6% of patients with Complete HELLP syndrome ,partial HELLP syndrome and preeclampsia respectively . 25% , 28% and 19% of patients with HELLP syndrome ,partial HELLP syndrome and preeclampsia had intra uterine growth restriction similar to joelciofransiscoAbbade et.al[10]

MATERNAL OUTCOME:
ECLAMPSIA occurred in 36.36% and 7.55% in patients with HELLP syndrome and preeclampsia respectively.

18.18% and 3.96% of patients with HELLP syndrome and preeclampsia had ACUTE RENAL FAILURE .

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MATERNAL MORTALITY was found in 18.18%, 6.25 % and 1.79 % of cases with HELLP syndrome, partial HELLP syndrome and preeclampsia.

As per our study , disseminated intravascular coagulation , acute renal failure were found to be important complications in patients with both HELLP syndrome and partial HELLP syndrome .Maternal mortality also seemed to be an important factor for the prognosis in the Complete HELLP syndrome group and partial HELLP syndrome group . All the above mentioned factors were found to be important prognostically in the study by Ching Ming Liu[13] et al.

CONCLUSION: Preeclampsia with severe features and eclampsia is common among the adolescents, unbooked , rural, and low socio-economic group of women in this study

There is need for policy makers to formulate policies toward ANC check up, awareness about danger signs of pregnancy by paramedical staff and provision of social amenities in rural areas

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