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META-ANALYSIS

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Corticosteroid Therapy for Management of Hemolysis, Elevated Liver Enzymes, and Low Platelet Count (HELLP) Syndrome: A Meta-Analysis

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Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
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Background: Hemolysis, elevated liver enzymes, and low platelet count (HELLP) syndrome is a severe condition of pregnancy that is associated with significant morbidity and mortality. Corticoteroid (CORT) therapy is common in the management of HELLP syndrome. This study evaluates the efficacy of CORT therapy to patients with HELLP Syndrome.

Material/Methods: A literature search was carried out in multiple electronic databases. Meta-analyses of means difference and odds ratio were carried under the random-effects model.

Results: Fifteen studies (675 CORT treated and 787 control HELLP patients) were included. CORT treatment significantly improved platelet count (mean difference between CORT treated and controls in changes from baseline, MD: 38.08 [15.71, 60.45]×10^9; p=0.0009), lactic dehydrogenase (LDH) levels (MD: –440 [–760, –120] IU/L; p=0.007), and alanine aminotransferase (ALT) levels (MD: –143.34 [–278.69, –7.99] IU/L; p=0.04) but the decrease in aspartate aminotransferase (AST) levels was not statistically significant (MD: –48.50 [–114.32, 17.32] IU/L; p=0.15). Corticosteroid treatment was also associated with significantly less blood transfusion rate (odds ratio, OR: 0.42 [0.24, 0.76]; p=0.004) and hospital/ICU stay (MD: –1.79 [–3.54, –0.05] days; p=0.04). Maternal mortality (OR: 1.27 [0.45, 3.60]; p=0.65), birth weight (MD: 0.09 [–0.11, 0.28]; p=0.38) and the prevalence of morbid conditions (OR: 0.79 [0.58, 1.08]; p=0.14) did not differ significantly between both groups.

Conclusions: Corticosteroid administration to HELLP patients improves platelet count, and the serum levels of LDH and ALT, and reduces hospital/ICU stay and blood transfusion rate, but is not significantly associated with better maternal mortality and overall morbidity.

MeSH Keywords: Enzyme Activators • Gestational Age • HELLP Syndrome • Hemolysis • Pregnancy Complications

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Background

Hemolysis, elevated liver enzymes, and low platelet count (HELLP) syndrome is a severe manifestation of a hypertensive disorder of pregnancy called pre-eclampsia. It affects about 10% to 20% of patients with severe pre-eclampsia (0.5% to 0.9% of all pregnancies) and causes significant mortality and morbidity, which increases in accordance with the severity of this syndrome [1,2]. This syndrome is associated with increased maternal risk of developing morbidities, including cerebrovascular complications, hemorrhage, pulmonary edema, retinal detachment, hematoma/ hepatic rupture, acute renal failure, liver failure, intravascular coagulopathy, placental abruption, and sepsis [3–5].

Perinatal/infant morbidity and mortality rates are higher in pregnant women with HELLP syndrome [6,7]. The preterm delivery rate is about 70% in HELLP syndrome patients with about 15% of cases requiring parturition before the 27th week of gestation [8]. HELLP syndrome has been found to incur long-term consequences as well. Sufferers may refrain from further pregnancies and need psychological support, and those who attempt further pregnancies have higher risk of gestational hypertension [9,10].

Previously, immediate delivery was indicated for patients diagnosed with HELLP syndrome, which often resulted in significant maternal and neonatal morbidity and/or mortality. Later it was recognized that antepartum administration of high-dose corticosteroids can stabilize the disease indicators and prolong the gestation [11]. Although many studies have demonstrated that CORT use helps raise the platelet count and reduce elevated liver enzymes, results are not consistent across all studies. Moreover, evidence regarding the role of corticosteroids in improving maternal morbidity and mortality is not clear. The present study, therefore, carried out a systematic review of the relevant studies and performed a meta-analysis of all related parameters for the sake of evaluating the efficacy of CORT therapy observed in studies with controlled designs.

Material and Methods

Important features of the method used for the present study are summarized in Table 1. Several electronic databases were searched for the acquisition of required study reports by using the most relevant MESH and keywords in different logical combinations and phrases. The inclusion criterion was 'the studies examining the efficacy of CORT therapy to treat HELLP patients either in a prospective or retrospective controlled design'. Some studies were, however, excluded by the following exclusion criteria (Table 1). Important information including outcome measures and outcomes, dosage and mode of administration of CORT, and obstetric and demographic characteristics were obtained from identified papers and organized on datasheets. Meta-analyses of mean difference and odds ratio were carried out under the random-effects model. Publication bias was assessed by visual examination of funnel plots.

Results

Fifteen studies [12–26] fulfilled were eligible and were included in the meta-analysis. A flowchart of the study screening and selection process is presented in Figure 1. Of the included studies, 8 were randomized controlled trials and 7 were retrospective analyses. The overall population of this meta-analysis is 675 CORT treated and 787 control HELLP patients. Age of the CORT treated and control patients as mean ±sd (range) was 26.94±5.8 (23.2±6–33.5±4) years and 26.35±5.7 (23.1±6–30.9±3.3) years, respectively. Gestation duration was 32.27±3.7 (29.1±3.5–35.1±2.9) weeks in CORT treated and 32.42±3.8 (27.6±3.3–35.5±2.6) weeks in control HELLP patients. In the CORT treated group, 42% of women were nulliparous, whereas 61% were nulliparous in the control group. Other characteristics of the included studies are presented in Supplementary Table 1. Least asymmetry was visible from the visual inspection of the funnel plots, indicative of almost no publication bias in this area of research (Figure 2).

Main findings of the meta-analysis are presented in Table 2. Corticosteroid treatment significantly increased platelet count in HELLP patients. The mean difference [95% confidence interval] in the change from baseline between CORT treated patients and controls was 38.08 [15.71, 60.45]×10^9/L; p=0.0009 (Figure 3). On the other hand, CORT treatment significantly decreased LDH and ALT levels. The mean differences in the changes from baseline between CORT treated and controls were –0.44 [–0.76, –0.12] IU/mL; p=0.007 for LDH (Figure 4) and –143.34 [–278.69, –7.99] IU/L; p=0.04 for ALT. However, the decrease in AST levels was not statistically significant in CORT-treated patients in comparison with controls (–48.50 [–114.32, 17.32] IU/L; p=0.15; Table 2).

Blood transfusion rate was significantly lower in CORT-treated patients (odds ratio [95% CI]: 0.42 [0.24, 0.76]; p=0.004. Hospital/ICU stay was also significantly lower in CORT-treated patients (mean difference: –1.79 [–3.54, –0.05]; p=0.04). There was no significant difference between CORT-treated and control patients in the incidence of cesarean deliveries (odds ratio [95% CI]: 1.25 [0.95, 1.63]; p=0.11), prevalence of infections (0.78 [0.19, 3.15]; p=0.73; Table 2), birth weight (mean difference: 0.09 [–0.11, 0.28]; p=0.38), infant respiratory distress incidence (odds ratio: 1.13 [0.50, 2.53]; p=0.78) and maternal mortality (odds ratio: 1.27 [0.45, 3.60]; p=0.65) (Table 2). Among the included studies, infant mortality was 23% in CORT-treated patients and 8.3% in controls [14] and 4% in CORT-treated

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Table 1. Important features of the method used in the present study.

Literature search	Databases including Embase, Google Scholar, Ovid SP, PubMed/Medline and ASI Web of Science were search for original research papers published before June 2015
MeSH terms and keywords	Hemolysis, elevated liver enzymes, and low platelet count/levels (HELLP) syndrome, corticosteroid therapy, dexamethasone, betamethasone, prednisolone, peripartum, antepartum, postpartum, lactic dehydrogenase, aspartate aminotransaminase, alanine transaminase
Type of studies	Prospective (randomized/non-randomized) or retrospective
Participants	HELLP syndrome patients admitted to the obstetric intensive care unit.
Interventions included	Studies evaluating the CORT therapy to treat antepartum/postpartum HELLP syndrome in controlled designs
Interventions excluded	Studies utilizing single arm designs; CORT utility for fetal lung maturity; CORT utility for eclampsia or pre-eclampsia; CORT utility in combination with other interventions such as platelets/heparin /plasma exchange etc.
Outcomes of interest	Changes from baseline in the platelets count, aspartate aminotransferase, alanine transferase, lactic dehydrogenase, blood pressure, and urinary output
HELLP definition used	Hemolysis as observed by an abnormal peripheral smear and lactate dehydrogenase (LDH) >600 IU/L, or total bilirubin >20.52 µmol/L; liver dysfunction indicated by aspartate transaminase (AST) >70 IU/L; and platelets <100,000 cells/mm^3 (Sibai 1993; Sibai 2004) Hemolysis indicated by an increased LDH level (over 600 IU/L) and progressive anemia; hepatic dysfunction as indicated AST >40 IU/L, an alanine transaminase (ALT) >40 IU/L, or both; and thrombocytopenia evidenced by a platelet nadir <150,000 cells/mm^3 (Martin 1999) Mississippi HELLP Classification System: HELLP 1: Platelet nadir ≤50,000 cells/mm^3; HELLP 2: Platelet nadir ≤100,000 cells/ mm^3; and HELLP 3: Platelet nadir ≤150,000 cells/ mm3 (Martin et al. 2006)
Data extraction	Independently by two authors. Inter-rater reliability: kappa=0.95
Meta-analysis	Calculation of mean differences in the percent changes from baseline in outcome measures followed by the calculation of overall effect size as a weighted average of the inverse variance adjusted individual study treatment effects under random-effects model (REM) Calculation of odds ratios for the incidence of cesarean delivery between CORT treated and control patients followed by the calculation of overall effect size (odds ratio) as a weighted average by using Mantel-Haenszel method Significance of difference between corticosteroid- and placebo-treated groups was tested by two-tailed z test
Heterogeneity	I^2 index used to assess between-study heterogeneity. Sensitivity analyses were performed to investigate the source of heterogeneity
Publication bias	Funnel plot asymmetry visual examination
Software	RevMan (Version 5.3; Cochrane Collaboration)

patients and 0% in controls [23]. Perinatal death was 0% in CORT-treated patients and 3% in controls [23].

Despite lower frequency of morbid conditions in HELLP patients treated with CORT (318 *vs.* 418), there was no significant difference in the incidence of overall morbidity between the groups (odds ratio: 0.79 [0.58, 1.08]; p=0.14). Morbid complications observed in 1 or more studies included pulmonary edema (3.6%) [12], intraventricular hemorrhage (18% [14,23], disseminated intravascular coagulation (15%) [18,22,26], endomyometritis (9%) [20], ascites (13.3%) [22], hematoma (3.3%) [22], acute renal failure and other renal pathologies (14% [17,18,22], necrotizing colitis (12% [23], bronchopulmonary dysplasia (80%) [23], intraventricular hematoma (20%) [23], infant thrombocytopenia (13%) [26], Apgar score less than 7 (18%) [14,23], and other hematological (36%) [17,22], neurological (12%) [17], and cardiopulmonary complications (33%) [17].

Discussion

This meta-analysis of the studies with variable research designs revealed that in comparison with controls, CORT therapy significantly improved the platelet count, LDH, and ALT, as well as reducing AST levels non-significantly in patients with HELLP syndrome. Moreover, blood transfusion rate and hospital/ICU stay were significantly lower in CORT-treated patients. However, there was no significant difference in the maternal mortality, overall morbidity, birth weight, or infant respiratory distress between CORT-treated and control patients.

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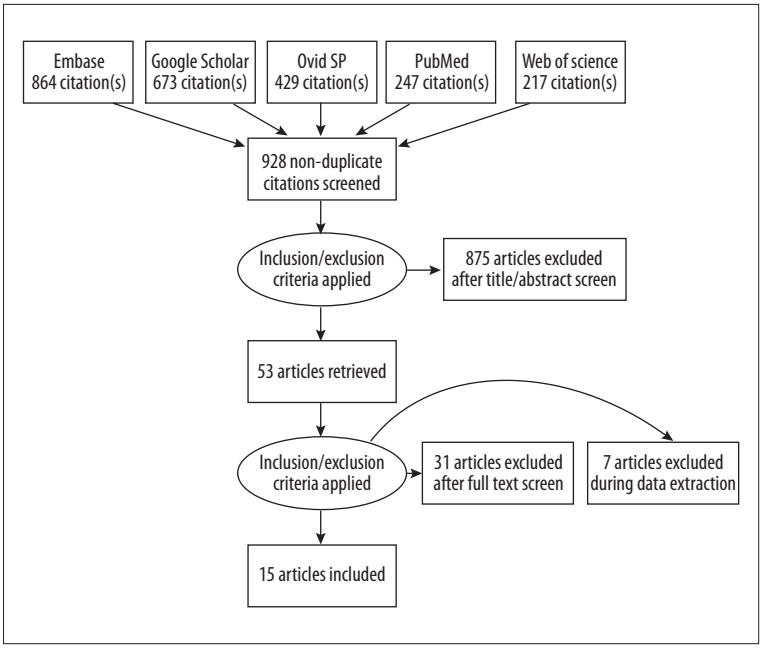

Figure 1. PRISMA flowchart of study screening and selection process.

Supplementary Table 1. Characteristics of the included studies.

Study	Design	Time	n		Gestation (CORT)		Gestation (controls)		Percent nulliparous	
			CORT	Control	Week	sd	Week	sd	CORT	Control
Fonseca 2005	RCT	Antepartum	66	66						
Katz 2008	DB-RCT	Postpartum	56	49	34.4	4.8	30.9	7.3	33	49
Magann 1994a	RCT	Antepartum	12	13	30.7	4.9	32.8	4.7	0	15
Magann 1994b	RCT	Postpartum	20	20	33.7	3.1	30.9	4.5		
Martin 1997	Retrospective	Postpartum	43	237						
Martin 2003	Retrospective	Peripartum	288	246	32	3.8	32	3.8	162	66
Meccai 2001	Retrospective	Postpartum	12	20	29.1	3.5	34.5	3.75	7	80
Nunes 2005	Retrospective	Peripartum	35	13	31.8	4.1	33	4.4	25	71
O'Brien 2000	Retrospective	Antepartum	11	11	32	5	36	2		
O'Brien 2002	Retrospective	Antepartum	46	23	32.4	3.4	34.8	4.8	36	65
Ozer 2009	RCT	Antepartum	30	30	32.4	4.5	33.1	3.7	15	60
van Runnard Heimel 2006	DB-RCT	Peripartum	15	16	27.4	1.4	27.6	3.3	14	81
Varol 2001	Retrospective	Postpartum	9	11	33.5	3.3	32.5	3.1		
Vigil-De Gracia 1997	RCT	Postpartum	17	17	32.82	3.42	34.41	2.81		
Yalcin 1998	RCT	Postpartum	15	15	35.1	2.9	35.5	2.6	10	60

Platelet count and serum LDH levels are reliable indicators of HELLP severity, and recovery and longer recovery time is required for more severe cases [27,28]. Corticosteroids are thought to prevent platelet consumption and erythrocyte destruction by stabilizing the vascular endothelium and effectually reducing blood product administration requirements

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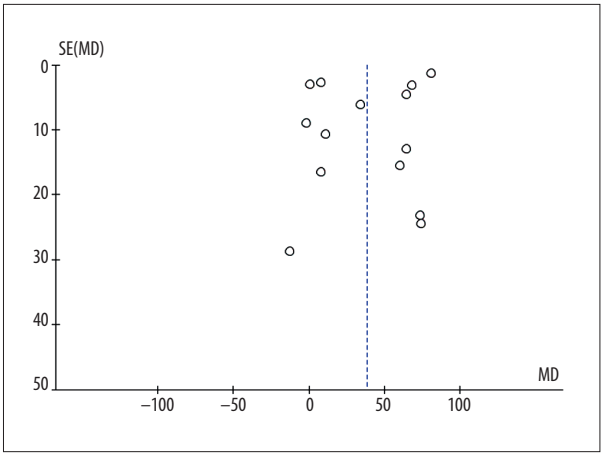

Figure 2. Funnel plot corresponding to the mean difference in the changes from baseline in platelet count.

[29,30]. The recovery of platelets is reported to start as earlier as 12 hours after CORT administration [31].

The HELLP syndrome, especially in the postpartum period, is associated with high maternal morbidity [32]. Class 1 HELLP syndrome patients are at higher risk of maternal mortality, and delay in the diagnosis worsens prognosis [33]. Despite improvements in biological parameters of HELLP syndrome, most of the studies reported that CORT treatment does not reduce maternal morbidity [34]. The present study also found no significant difference between CORT-treated and control HELLP patients in the incidence of overall morbidity in a meta-analysis of 8 studies presenting 15 morbid conditions. However, the frequency of events was considerably less in CORT-treated patients. Data were not sufficient for the evaluation of all morbid conditions individually. There was also no significant difference between both the groups in maternal mortality. The morbid conditions observed in the present study were also reported by many studies not included in this meta-analysis [32,33]. The morbidities not reported herein include abruptio placentae, retinal detachment, adult respiratory distress syndrome, and hypoxic ischemic encephalopathy [32,33].

The etiology of the HELLP syndrome is poorly understood. It is believed that an imbalance between proangiogenic and antiangiogenic factors and increased proinflammatory cytokines play an important role in women with preeclampsia and HELLP

Table 2. Main findings of the meta-analysis.

Parameter	Studies/patients	Mean difference [95% CI]	p	I^2/I^2 after sensitivity analysis
Platelet count (×10⁹/L)	10/1315	38.08 [15.71, 60.45]	p=0.0009	99%/82%
LDH (IU/mL)	10/1162	–0.44 [–0.76, –0.12]	p=0.007	94%/76%
AST (IU/L)	8/755	–48.50 [–114.32, 17.32]	p=0.15	92%/90%
ALT (IU/L)	4/179	–143.34 [–278.69, –7.99]	p=0.04	99%/87%
SBP (mm Hg)	3/125	2.10 [–7.71, 11.91]	p=0.67	63%/21%
DBP (mm Hg)	3/125	–2.88 [–8.24, 2.47]	p=0.29	60%/23%
Birth weight (kg)	3/116	0.09 [–0.11, 0.28]	p=0.38	63%/21%
Hospital/ICU stay (days)	7/410	–1.79 [–3.54, –0.05]	p=0.04	64%/30%
Parameter	**Studies/patients**	**Odds ratio [95% CI]**	**p**	**I^2/I^2 after sensitivity analysis**
Cesarean delivery	9/1142	1.25 [0.95, 1.63]	p=0.11	0%
Blood transfusion	4/217	0.42 [0.24, 0.76]	p=0.004	3%
Overall morbidity*	8/866	0.79 [0.58, 1.08]	p=0.14	53%
Infant respiratory distress	5/1000	1.13 [0.50, 2.53]	p=0.78	78%
Infections	3/600	0.78 [0.19, 3.15]	p=0.73	82%/0%
Maternal mortality	7/893	1.27 [0.45, 3.60]	p=0.65	0%

ALT – alanine aminotransferase; AST – aspartate aminotransferase; CI – confidence interval; DBP – diastolic blood pressure; I^2 – between study statistical heterogeneity index; ICU – intensive care unit; IU/L – international units per liter; LDH – lactic dehydrogenase. * Morbid conditions are described in results section.

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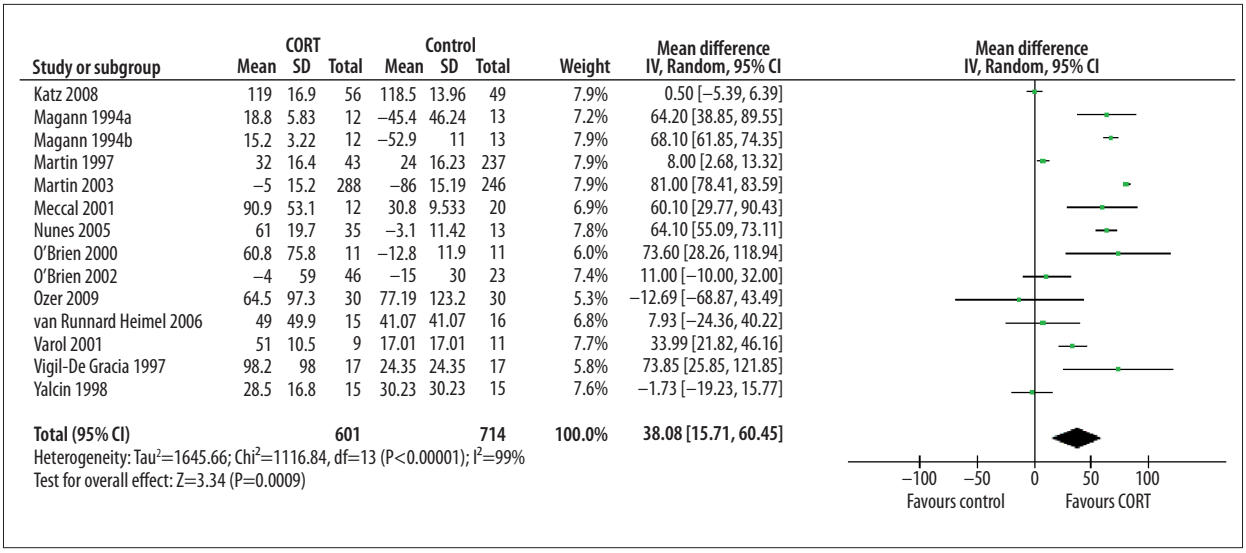

Figure 3. Forest graph showing the effect of CORT on platelet count in individual studies and the overall effect of the meta-analysis.

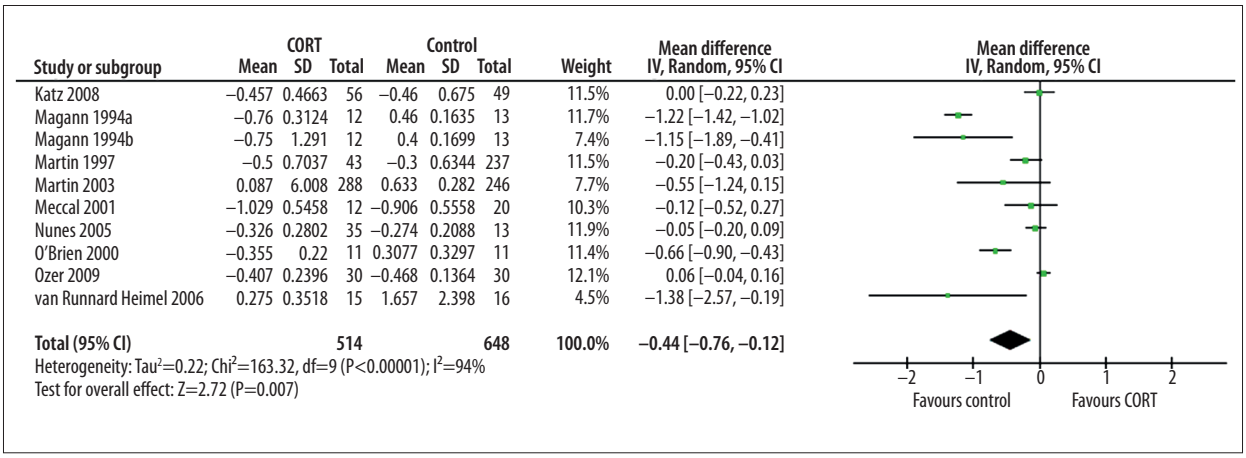

Figure 4. Forest graph showing the effect of CORT on LDH in individual studies and the overall effect of the meta-analysis.

syndrome. Higher circulating levels of anti-angiogenic proteins secreted by the placenta, such as soluble fms-like tyrosine kinase 1 (sFlt1) and soluble endoglin, are found in preeclampsia patients [35]. Dexamethasone has been demonstrated to significantly decrease sFlt-1, soluble endoglin, IL-6, and TNF-α after 24 hours of treatment in HELLP patients. These soluble factors are known to stimulate angiotensin II receptor (AT1-AA) production and increase endothelin 1, which are known to play a pathophysiological role in gestational hypertension [36]. These findings suggest that targeting immunomodulators of HELLP syndrome pathology may be a novel therapeutic research strategy.

Management of HELLP syndrome requires earlier diagnosis, mother-fetus status examination, stabilization of the indicators and symptoms, delivery at optimal time, and postpartum care in order to reduce maternal morbidity and mortality. A rather longer postpartum recovery period may be required for patients with progressively worsening HELLP syndrome [27]. Corticosteroid therapy is a cost-effective medication that can be administered via different routes and reduces the length of hospitalization as compared to other treatments, such as platelet transfusion [3]. In the present study, on average, CORT therapy reduced hospital/ICU stay by about 3 days in comparison with controls and this difference was statistically significant in the meta-analysis of 7 studies. Thus, corticosteroids can be beneficial in carefully selected HELLP patients without apparent adverse effects to mother or fetus/neonate.

This meta-analysis has some important limitations. Firstly, studies with varying designs were included because none of a particular design could make sufficient data available. Secondly, clinical and methodological heterogeneity of the sample population in the form of factors such as the severity of HELLP syndrome, time of CORT administration, and dosage and duration of CORT administration in recruited patients may have

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affected overall outcomes. Although, the random-effects model was used to interpret the results, but multi-center randomized controlled trials will be required for clarification of these results. Thirdly, the effect of some statistical procedures used to impute missing data may also have had a slight impact, as not all studies provided measures of dispersal values of the effect size of change in indicators following CORT/placebo treatments.

Conclusions

Corticosteroid administration to HELLP patients improves platelet count and the serum levels of LDH, besides reducing hospital/ICU stay and blood transfusion rate. However, these indices are not significantly associated with maternal mortality and overall morbidity prevalence.

References:

1. Martin JN Jr, Rose CH, Briery CM: Understanding and managing HELLP syndrome: the integral role of aggressive glucocorticoids for mother and child. Am J Obstet Gynecol, 2006; 195(4): 914–34
2. Haram K, Svendsen E, Abildgaard U: The HELLP syndrome: clinical issues and management. A Review. BMC Pregnancy Childbirth, 2009; 9: 8
3. Vigil-De Gracia P: HELLP syndrome. Ginecol Obstet Mex, 2015; 83(1): 48–57
4. Martin JN Jr, Blake PG, Lowry SL et al: Pregnancy complicated by preeclampsia-eclampsia with the syndrome of hemolysis, elevated liver enzymes, and low platelet count: how rapid is postpartum recovery? Obstet Gynecol, 1990; 76: 737–41
5. Sibai BM, Ramadan MK, Usta I et al: Maternal morbidity and mortality in 442 pregnancies with hemolysis, elevated liver enzymes, and low platelets (HELLP syndrome). Am J Obstet Gynecol, 1993; 169(4): 1000–6
6. Witlin AG, Saade GR, Mattar F, Sibai BM: Predictors of neonatal outcome in women with severe preeclampsia or eclampsia between 24 and 33 weeks' gestation. Am J Obstet Gynecol, 2000; 182: 607–11
7. Tompkins MJ, Thiagarajah S: HELLP (hemolysis, elevated liver enzymes, and low platelet count) syndrome: the benefit of corticosteroids. Am J Obstet Gynecol, 1999; 181: 304–9
8. Abramovici D, Friedman SA, Mercer BM et al: Neonatal outcome in severe preeclampsia at 24 to 36 weeks' gestation: does the HELLP (hemolysis, elevated liver enzymes, and low platelet count) syndrome matter? Am J Obstet Gynecol, 1999; 180(1 Pt 1): 221–25
9. van Pampus MG, Wolf H, Mayruhu G et al: Long-term follow-up in patients with a history of (H)ELLP syndrome. Hypertens Pregnancy, 2001; 20(1): 15–23
10. Chames MC, Haddad B, Barton JR et al: Subsequent pregnancy outcome in women with a history of HELLP syndrome at < or =28 weeks of gestation. Am J Obstet Gynecol, 2003; 188(6): 1504–7; discussion 1507–8
11. Heller CS, Elliott JP: High-order multiple pregnancies complicated by HELLP syndrome. A report of four cases with corticosteroid therapy to prolong gestation. J Reprod Med, 1997; 42(11): 743–46
12. Fonseca JE, Mendez F, Catano C, Arias F: Dexamethasone treatment does not improve the outcome of women with HELLP syndrome: a double-blind, placebo-controlled, randomized clinical trial. Am J Obstet Gynecol, 2005; 193(5): 1591–98
13. Katz L, de Amorim MM, Figueiroa JN et al: Postpartum dexamethasone for women with hemolysis, elevated liver enzymes, and low platelets (HELLP) syndrome: a double-blind, placebo-controlled, randomized clinical trial. Am J Obstet Gynecol, 2008; 198(3): 283.e1–8
14. Magann EF, Bass D, Chauhan SP et al: Antepartum corticosteroids: disease stabilization in patients with the syndrome of hemolysis, elevated liver enzymes, and low platelets (HELLP). Am J Obstet Gynecol, 1994; 171(4): 1148–53
15. Magann EF, Perry KG Jr, Meydrech EF et al: Postpartum corticosteroids: accelerated recovery from the syndrome of hemolysis, elevated liver enzymes, and low platelets (HELLP). Am J Obstet Gynecol, 1994; 171(4): 1154–58
16. Martin JN Jr, Perry KG Jr, Blake PG et al: Better maternal outcomes are achieved with dexamethasone therapy for postpartum HELLP (hemolysis, elevated liver enzymes, and thrombocytopenia) syndrome. Am J Obstet Gynecol, 1997; 177(5): 1011–17
17. Martin JN Jr, Thigpen BD, Rose CH et al: Maternal benefit of high-dose intravenous corticosteroid therapy for HELLP syndrome. Am J Obstet Gynecol, 2003; 189(3): 830–34
18. Mecacci F, Carignani L, Cioni R et al: Time course of recovery and complications of HELLP syndrome with two different treatments: heparin or dexamethasone. Thromb Res, 2001; 102(2): 99–105
19. Nunes F, Campos AP, Avillez T et al: Corticosteroid therapy for patients with HELLP syndrome (hemolysis, elevated liver enzymes, and low platelet count). Acta Med Port, 2005; 18(3): 177–82
20. O'Brien JM, Milligan DA, Barton JR: Impact of high-dose corticosteroid therapy for patients with HELLP (hemolysis, elevated liver enzymes, and low platelet count) syndrome. Am J Obstet Gynecol, 2000; 183(4): 921–24
21. O'Brien JM, Shumate SA, Satchwell SL et al: Maternal benefit of corticosteroid therapy in patients with HELLP (hemolysis, elevated liver enzymes, and low platelet count) syndrome: impact on the rate of regional anesthesia. Am J Obstet Gynecol, 2002; 186(3): 475–79
22. Ozer A, Kanat-Pektas M, Ozer S et al: The effects of betamethasone treatment on clinical and laboratory features of pregnant women with HELLP syndrome. Arch Gynecol Obstet, 2009; 280(1): 65–70
23. van Runnard Heimel PJ, Huisjes AJ, Franx A et al: A randomised placebo-controlled trial of prolonged prednisolone administration to patients with HELLP syndrome remote from term. Eur J Obstet Gynecol Reprod Biol, 2006; 128(1–2): 187–93
24. Varol F, Aydin T, Gucer F: HELLP syndrome and postpartum corticosteroids. Int J Gynaecol Obstet, 2001; 73(2): 157–59
25. Vigil-De Gracia P, García-Cáceres E: Dexamethasone in the post-partum treatment of HELLP syndrome. Int J Gynaecol Obstet, 1997; 59(3): 217–21
26. Yalcin OT, Sener T, Hassa H et al: Effects of postpartum corticosteroids in patients with HELLP syndrome. Int J Gynaecol Obstet, 1998; 61(2): 141–48
27. Martin JN Jr, Blake PG, Lowry SL et al: Pregnancy complicated by preeclampsia-eclampsia with the syndrome of hemolysis, elevated liver enzymes, and low platelet count: how rapid is postpartum recovery? Obstet Gynecol, 1990; 76(5 Pt 1): 737–41
28. Rinehart BK, Terrone DA, May WL et al: Change in platelet count predicts eventual maternal outcome with syndrome of hemolysis, elevated liver enzymes and low platelet count. J Matern Fetal Med, 2001; 10(1): 28–34
29. Martin JN Jr, Files JC, Blake PG et al:Postpartum plasma exchange for atypical preeclampsia-eclampsia as HELLP (hemolysis, elevated liver enzymes, and low platelets) syndrome. Am J Obstet Gynecol, 1995; 172(4 Pt 1): 1107–25; discussion 1125–27
30. Isler CM, Barrilleaux PS, Magann EF et al: A prospective, randomized trial comparing the efficacy of dexamethasone and betamethasone for the treatment of antepartum HELLP (hemolysis, elevated liver enzymes, and low platelet count) syndrome. Am J Obstet Gynecol, 2001; 184(7): 1332–37; discussion 1337–39
31. Crane JM, Tabarsi B, Hutchens D: The maternal benefits of corticosteroids with HELLP (hemolysis, elevated liver enzymes, low platelet count) syndrome. J Obstet Gynaecol Can, 2003; 25(8): 650–55
32. Sibai BM, Ramadan MK, Usta I et al: Maternal morbidity and mortality in 442 pregnancies with hemolysis, elevated liver enzymes, and low platelets (HELLP syndrome). Am J Obstet Gynecol, 1993; 169(4): 1000–6
33. Isler CM, Rinehart BK, Terrone DA et al: Maternal mortality associated with HELLP (hemolysis, elevated liver enzymes, and low platelets) syndrome. Am J Obstet Gynecol, 1999; 181(4): 924–28
34. Bouchnak M, Souissi K, Ouragini H et al: Maternal benefit of postpartum corticosteroid therapy in patients with HELLP (hemolysis elevated liver enzymes low platelets count) syndrome. Tunis Med, 2005; 83(8): 473–76
35. Steinberg G, Khankin EV, Karumanchi SA: Angiogenic factors and preeclampsia. Thromb Res, 2009; 123(Suppl.2): S93–99
36. Wallace K, Martin JN Jr, Tam Tam K et al: Seeking the mechanism(s) of action for corticosteroids in HELLP syndrome: SMASH study. Am J Obstet Gynecol, 2013; 208(5): 380.e1–8

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