



www.figo.org

Contents lists available at ScienceDirect

International Journal of Gynecology and Obstetrics

journal homepage: www.elsevier.com/locate/ijgo



REVIEW ARTICLE

Maternal deaths due to eclampsia and HELLP syndrome

Paulino Vigil-De Gracia*

Critical Care Unit, Department of Obstetrics and Gynecology, Caja de Seguro Social, Panama, Panama

ARTICLE INFO

Article history:

Received 6 August 2008

Received in revised form 1 September 2008

Accepted 5 September 2008

Keywords:

Eclampsia

HELLP syndrome

Maternal mortality

Pre-eclampsia/eclampsia

ABSTRACT

Objective: To evaluate maternal deaths associated with eclampsia, HELLP syndrome, and the concurrence of these conditions. **Method:** A review of Medline studies reporting maternal deaths associated with eclampsia or HELLP syndrome published in English, Spanish, and Portuguese between 1995 and June 2008. **Results:** A total of 304 deaths were identified: 100 due to eclampsia, 117 due to eclampsia/HELLP, and 87 associated with HELLP syndrome. Of the total deaths, 71.3% of women had seizures and 67.1% developed HELLP syndrome. In high-income countries 3.9% of deaths were due to eclampsia without HELLP syndrome, while in low-income countries this figure was 42.5% ($P < 0.0001$). The presence of HELLP syndrome in the women who died of eclampsia was 90.6% (29/32) in high-income countries compared with 47.6% (88/185) in low-income countries ($P < 0.001$). **Conclusion:** Concurrent eclampsia and HELLP syndrome was diagnosed in 5–6 out of 10 deaths associated with eclampsia or HELLP syndrome in this review.

© 2008 International Federation of Gynecology and Obstetrics. Published by Elsevier Ireland Ltd. All rights reserved.

1. Introduction

Each year approximately 63 000 women worldwide die of eclampsia and pre-eclampsia, and 99% of these deaths occur in low-income countries [1]. Eclampsia is defined as the occurrence of seizures in a woman with pre-eclampsia that cannot be attributed to other causes. The reported maternal mortality rates from eclampsia range from 0% to 1.8% in some centers in high-income countries [2,3] to as high as 15% in Nigeria and Bangladesh [4,5].

HELLP syndrome represents a severe form of pre-eclampsia/eclampsia characterized by hemolysis, elevated liver enzymes, and low platelets [6]. The reported maternal mortality rates from HELLP syndrome range from 1% in the United States [7] to 30% in Turkey [8].

It has been theorized that eclampsia is the natural linear evolution of pre-eclampsia. Eclampsia, however, can manifest without warning or signs of pre-eclampsia and, in a retrospective analysis by Katz et al. [2], eclampsia was not found to progress from pre-eclampsia. Endothelial dysfunction is considered central to the multiple-organ pathophysiology of pre-eclampsia/eclampsia, and microangiopathic hemolysis, which suggests endothelial damage, is characteristic of HELLP syndrome. The reported incidence of HELLP syndrome in association with eclampsia ranges from 10.8% to 32.1% [9,10], and the incidence of eclampsia in association with HELLP syndrome ranges from 6% to 52% [7,11]. However, maternal mortality associated with a concurrent condition (HELLP/eclampsia [HE] or eclampsia/HELLP [EH]) has not been fully analyzed.

The present review was carried out to investigate the trends in maternal deaths due to eclampsia, HELLP syndrome, or a concurrent

condition (HE/EH) to assess whether there is an association or change of paradigm, which may help to prevent maternal mortality from hypertensive disorders of pregnancy.

2. Material and methods

A review of the English, Spanish, and Portuguese language literature was undertaken using Medline to identify reports of maternal deaths associated with eclampsia, HELLP syndrome, or concurrent conditions published between January 1995 and June 2008. The search terms were: “eclampsia maternal mortality;” “eclampsia deaths;” “HELLP syndrome maternal mortality;” “HELLP deaths;” “microangiopathic hemolytic anemia deaths;” “eclampsia HELLP syndrome deaths;” and “eclampsia HELLP syndrome maternal mortality.” We also searched the reference lists of the identified articles and selected those that reported deaths associated with eclampsia or HELLP syndrome during the period of study. Publications documenting maternal deaths were reviewed and all deaths of patients with eclampsia (with or without HELLP syndrome) or deaths of patients with HELLP syndrome were included in the analysis. Eclampsia was defined as convulsions or seizures during pregnancy or the postpartum period in a woman with pre-eclampsia that could not be attributed to other causes. HELLP syndrome was determined by the presence of thrombocytopenia ($< 100\ 000$ cells/ μL), hemolysis, and hepatic dysfunction (elevated transaminases and lactic dehydrogenase activities).

Concurrent HELLP/eclampsia (HE) or eclampsia/HELLP (EH) were defined as the presence of eclampsia and HELLP syndrome in a maternal death; in this review these conditions are referred to as HE/EH.

Each case report or series was reviewed for eclampsia, HELLP syndrome, HE/EH, country, and cause of death. In articles where the information about concurrent eclampsia and HELLP syndrome was unclear, the authors were contacted to provide further details. Papers

* Apartado Postal: 0823-03828, Panama, Panama. Tel.: +507 66143240.
E-mail address: pvigild@hotmail.com.

reporting deaths related to eclampsia without reports on HELLP syndrome were excluded; this scenario is common before 1995, especially in low-income countries. Some publications reported HELLP syndrome as the cause or primary cause of death, but when the cause of death was “other” or there was an absence of information, these articles were excluded. In studies where there was partial data duplication with some cases overlapping between different publications, the most complete and largest dataset was selected.

Review of all deaths made it possible to compare and contrast groups according to occurrence in high-income or low-income countries, and publications in English or Spanish. High-income countries were defined as countries with a gross national income per capita of US \$11,116 or greater, while low-income countries were defined as countries with a national income per capita of less than US \$11,116.

Results are reported as numbers and percentages. Fisher exact test and χ^2 test were used to test categorical variables. $P < 0.05$ was considered statistically significant.

3. Results

The search strategy yielded 44 publications describing cases of maternal mortality associated with eclampsia, HELLP syndrome, and HE/EH that met the full inclusion criteria (Fig. 1). Eight publications

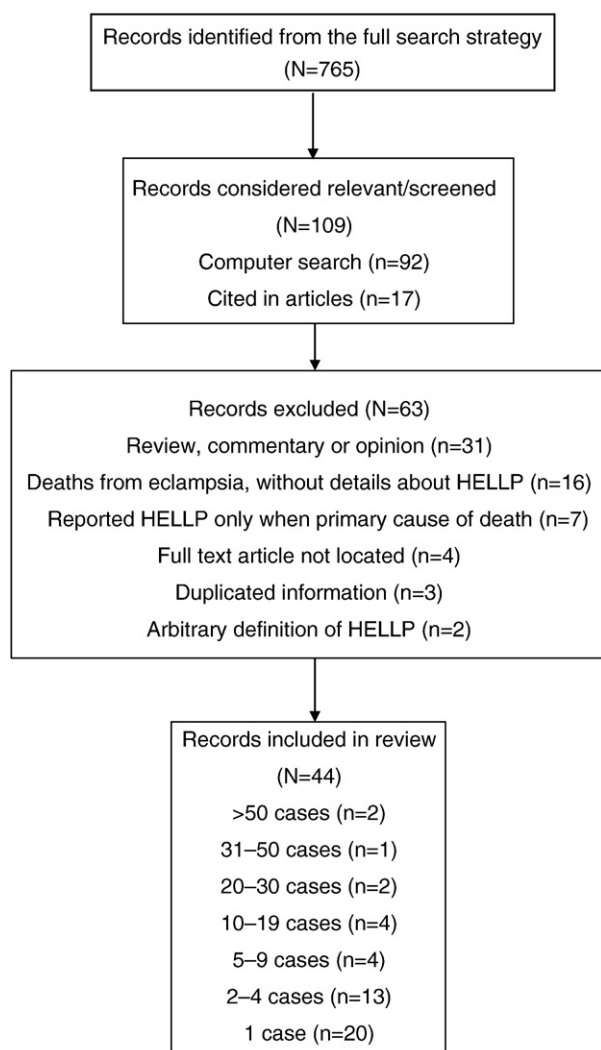


Fig. 1. Flow chart of studies selected for the review.

Table 1

Distribution of maternal mortality due to eclampsia, HE/EH, and HELLP syndrome

Author	Year	Country	Deaths	Eclampsia	HE/EH	HELLP
Vigil-De Gracia et al. [12] ^a	1996	Mexico	14	5	–	9
Helguera et al. [13] ^a	1996	Mexico	20	6	9	5
Vigil-De Gracia and García-Cáceres [14]	1997	Mexico	1	–	–	1
Vigil-De Gracia [15]	1998	Panama	5	1	3	1
Conde-Agudelo and Kafury-Goeta [16]	1998	Colombia	10	6	4	–
Wijesinghe et al. [17]	1998	Sri Lanka	3	–	1	2
Onrust et al. [18] ^c	1999	Netherlands	2	–	1	1
Sheikh et al. [19] ^c	1999	EUA	1	–	–	1
Lara et al. [20] ^a	1999	Mexico	37	20	17	–
Isler et al. [6] ^c	1999	EUA	52	–	23	29
Haddad et al. [7] ^c	2000	EUA	2	–	–	2
Mattar and Sibai [9] ^c	2000	EUA	2	2	–	–
Reck et al. [21] ^c	2001	Germany	1	–	–	1
Romero et al. [22] ^a	2001	Mexico	8	–	6	2
Tank et al. [23]	2001	India	6	–	3	3
Vigil-De Gracia [24]	2001	Panama	2	–	1	1
Soh et al. [25] ^c	2002	Japan	1	–	–	1
Vigil-De Gracia et al. [26] ^a	2002	C-America	7	1	6	–
Juarez-Azpilcueta et al. [27] ^a	2003	Mexico	2	–	–	2
Ding et al. [28] ^c	2003	Taiwan	1	–	–	1
Knopp et al. [29] ^c	2003	Germany	1	–	–	1
Capellino et al. [30] ^a	2003	Argentina	1	–	–	1
Rodríguez et al. [31] ^a	2003	Mexico	1	–	–	1
Agarwal et al. [32]	2003	India	1	–	1	–
Chen et al. [33] ^c	2003	Singapore	1	1	–	–
Coelho [34] ^b	2004	Brazil	1	1	–	–
Oettle et al. [35]	2005	South Africa	1	–	–	1
Nunes et al. [36] ^c	2005	EUA	1	–	–	1
Zeidman et al. [37] ^c	2005	EUA	1	–	–	1
Yücesoy et al. [38]	2005	Turkey	3	–	1	2
Fonseca et al. [39]	2005	Colombia	4	–	1	3
Osmanagaoglu et al. [8]	2006	Turkey	11	–	11	–
Demir et al. [40]	2006	Turkey	2	–	2	–
Heimel et al. [41] ^c	2006	Netherlands	1	–	–	1
Araujo et al. [42]	2006	Brazil	1	–	1	–
Gaugler-Sende et al. [43] ^c	2006	Netherlands	1	–	1	–
Minkauskiene et al. [44]	2006	Lithuania	1	–	–	1
Dissanayake et al. [45]	2007	Sri Lanka	1	–	1	–
Chhabra and Kakani [46]	2007	India	45	29	10	6
Gómez-Puerta et al. [47] ^c	2007	Spain	4	–	–	4
Efetie and Okafor [48]	2007	Nigeria	13	7	6	–
Miguil and Chekairi [49]	2008	Morocco	23	21	2	–
Zwart et al. [3] ^c	2008	Netherlands	4	–	4	–
Katz et al. [50]	2008	Brazil	4	–	2	2
Total			304	100 (32.9)	117 (38.5)	87 (28.6)

Abbreviation: HE/EH; HELLP/eclampsia and eclampsia/HELLP.

^a In Spanish.

^b In Portuguese.

^c High-income country.

were in Spanish, 1 in Portuguese, and 35 in English; 16 of the papers in English were from high-income countries [3,6–9,12–50] (Table 1).

A total of 304 maternal deaths were identified. One hundred (32.9%) deaths were due to eclampsia, 117 (38.5%) deaths were from HE/EH, and 87 (28.6%) deaths were related solely to HELLP syndrome.

Table 2

Maternal mortality by country income status and publication language^a

Variable	Total deaths	Eclampsia	HE/EH	HELLP	P value
Country status					
High-income	76	3 (3.9)	29 (38.1)	44 (58)	0.0001
Low-income	228	97 (42.5)	88 (38.6)	43 (18.9)	
Publication language					
Spanish ^b	91	33 (36.2)	38 (41.8)	20 (22)	0.14
English	213	67 (31.4)	79 (37.1)	67 (31.5)	

Abbreviation: HE/EH; HELLP/eclampsia and eclampsia/HELLP.

^a Values are given as number (percentage).

^b One study was in Portuguese.

Table 3
Causes of maternal mortality by group

Cause of mortality	Eclampsia n=70 (70%) ^a	HE/EH n=47 (40.2%) ^a	HELLP n=60 (69.0%) ^a
First	Cerebral hemorrhage (43%)	Cerebral hemorrhage (44%)	Cerebral hemorrhage (27%)
Second	Renal Failure (26%)	SIRPA (13%)	SIRPA (22%)
Third	DIC (11%)	Cerebral Edema (10%)	Liver Rupture (17%)
Fourth	Cerebral Edema (4%)	MOF (10%)	MOF (12%)

Abbreviations: HE/EH, HELLP/eclampsia and eclampsia/HELLP; ARDS, adult respiratory distress syndrome; DIC, disseminated intravascular coagulation; MOF, multiple organ failure.

^a Percentage obtained from total deaths by group.

Of the total deaths, 217 (71.3%) women had seizures and of these, 117 (53.9%) had HELLP syndrome. Of the total deaths, 204 (67.1%) had HELLP syndrome, of which 117 (57.3%) developed convulsions (Table 2).

Seventy-six deaths were in high-income countries. Three (3.9%) of these were due to eclampsia without HELLP syndrome; conversely, in low-income countries 97 deaths (42.5%) were due to eclampsia without HELLP syndrome ($P<0.0001$; Table 2). Of the deaths in high-income countries, a total of 73 (96%) women developed HELLP syndrome, while in contrast a total of 131 (57.4%) women in low-income countries developed HELLP syndrome. The presence of HELLP syndrome in the women who had eclampsia or convulsions was 90.6% (29/32) in high-income countries compared with 47.6% (88/185) in low-income countries ($P<0.001$). On the other hand, the presence of eclampsia in the women with HELLP was 40% (29/73) in high-income countries and 67.1% (88/131) in low-income countries ($P<0.001$).

The comparison of contributing conditions among publications in English or Spanish/Portuguese was not significant ($P=0.14$).

The most common primary cause of maternal death among the 3 groups was intracranial hemorrhage, and the other causes were varied (Table 3).

4. Discussion

In this review, eclampsia with HELLP syndrome as a concurrent condition was present in 5–6 out of 10 deaths associated with eclampsia or HELLP syndrome. The ratio of deaths associated with eclampsia was higher in low-income countries at 6:1 (85% vs 15%). Our findings confirm the prominent role of eclampsia as a cause of maternal death in low-income countries [2,4,5]. Interestingly, concurrent eclampsia with HELLP syndrome represents the principal cause or contributing condition for eclampsia-related mortality in high-income countries. Therefore, developing HELLP syndrome places any woman at significant risk of mortality. It might then be possible to reduce maternal mortality from eclampsia by earlier diagnosis, and by recognition and treatment of HELLP syndrome.

Maternal mortality related to eclampsia without HELLP syndrome might be reduced as a result of some strategies, as evidenced by the lower death rate of 9.4% in high-income countries. Death caused by the concurrent conditions (HE/EH) is a serious problem in both high- and low-income countries, and contributes significantly to maternal deaths associated with pre-eclampsia/eclampsia. Of the total mortalities associated with eclampsia, HELLP syndrome was present in approximately 54% (117/217). Our findings suggest that in cases of maternal mortality caused by eclampsia, management of women with pre-eclampsia was not the main goal, although it may be true in patients with HELLP syndrome. Vigil-De Gracia and García-Cáceres [51] reported that thrombocytopenia was a highly predictive factor of death in women with eclampsia. However, they did not analyze the presence or absence of HELLP syndrome. Recently, Schutte et al. [52] and Miguil and Chekairi [49] reported similar outcomes. Therefore, when eclampsia-related death occurs, it is likely to be associated with

HELLP syndrome rather than seizure alone. This is an important point not analyzed in the MAGPIE study [53] and may partly explain why there is no difference in maternal mortality among the countries studied. Therefore, the control or absence of control of seizures did not appear to affect the cause or timing of death in patients without HELLP syndrome.

Because of restricted maternity services in low-income countries, poor transport systems, cultural practices and other factors, women infrequently attend prenatal care or do not attend until late in pregnancy. Lack of prenatal care is associated with a large number of deaths caused by eclampsia. Furthermore, many women with eclampsia are not evaluated for HELLP syndrome in low-income countries for many reasons, such as eclampsia and death occurring before patients reach hospital; it is not possible to obtain platelet counts; lack of laboratory services; lack of appropriately trained staff; and incorrect diagnosis [54]. On the other hand, eclampsia is easy to diagnose, and this could explain the prevalence of eclampsia without HELLP syndrome in low-income countries. In both high- and low-income countries, HELLP syndrome is reported as a primary cause or specific cause of death in pregnancies complicated by hypertension [54,55]. Thus, some deaths caused by eclampsia with HELLP syndrome are reported as death caused by eclampsia or pre-eclampsia/eclampsia only [52,56].

The reported incidence of HELLP syndrome in association with eclampsia, and of eclampsia in association with HELLP syndrome varies [7,9–11]. Approximately 16% of cases of HELLP syndrome are reported in association with eclampsia [9,10,16,24], and 10% of eclampsia cases in association with HELLP syndrome [7,10,11,24]. The present review found a constant relationship between the concurrent conditions (HE/EH) and maternal mortality, which is similar to other studies [18]. HELLP syndrome is the most important factor concurrent with seizures associated with death from pre-eclampsia/eclampsia in high- and low-income countries between 1995 and 2008. It was unexpected to find that HELLP syndrome was a more important factor associated with maternal mortality than convulsions in high-income countries; however, in low-income countries eclampsia still dominates. A study from the United States [2] has reported eclampsia without associated death. However, in the USA there are approximately 30 deaths due to eclampsia every year [57]. According to the results of the present review, about 17 deaths each year are associated with eclampsia and concurrent HELLP syndrome in the USA.

Globally, it is possible that deaths from HELLP syndrome are reported as deaths from pre-eclampsia or eclampsia. It is more accurate to describe HELLP syndrome as a serious multisystem disease, involving the central nervous system [6,7,26,29,31,37,39,49,55,58], lungs [37], liver [6,7,10,18,21,42], and kidney damage [6–8,10,12,20,46,48]. In some cases the specific cause of death is associated with the failure of one vital organ (cerebral hemorrhage, liver rupture); however in other cases the cause of death is multiple organ failure [6,8,20,23,46,51].

The findings of this analysis reveal that the majority of maternal deaths were due to intracerebral hemorrhage. This finding is similar to previous reports [6,51,52,56]. Cerebrovascular events in eclampsia appear to constitute a continuum characterized by an initial, reversible phase of vasogenic edema and seizures caused by hypertension, along with endothelial dysfunction [58]. The endothelial dysfunction present with HELLP syndrome may injure the normal protective blood–brain barrier systems in the brain while also causing or contributing to higher blood pressures [59]. Furthermore, the presence of HELLP syndrome is associated with an increased risk of disseminated intravascular coagulation and this may contribute to cerebral hemorrhages. The prevention of the occurrence of multiple seizures seems important because the large majority of women with multiple seizures had evidence of cerebral infarction and HELLP syndrome [58].

The dangers of high systolic or diastolic blood pressure in combination with HELLP syndrome or thrombocytopenia and seizures

(known as the “dangerous triad”) [51], seems to be deeply underestimated in relation to intracerebral hemorrhage and maternal death due to eclampsia. This is supported by the present study and 5 other recent publications [49,51,52,56,59]. Schutte et al. [52] reported 27 deaths due to hypertensive disorders, of which 60% had eclampsia, 52% had platelet counts below 100 000 cells/uL, diastolic blood pressure was ≥ 110 mm Hg in 64%, and systolic blood pressure was ≥ 160 mm Hg in all of the women. Martin et al. [59] reported 28 cases of stroke and pre-eclampsia/eclampsia, of which 18 had HELLP syndrome and 8 presented with eclampsia [59]. They reported a systolic blood pressure threshold of approximately 155–160 mm Hg. Fifteen patients died following a stroke. Miguil and Chekairi [49] reported 23 deaths due to eclampsia, 61% had cerebral hemorrhage or ischemia, the mean platelet count was 105 000 cells/ μ L, and over 50% had severe systolic and diastolic blood pressures. A UK study [56] reported 18 deaths caused by pre-eclampsia/eclampsia: 44.4% had HELLP syndrome and 33.3% presented with eclampsia. Vigil-De Gracia [51] reported the dangerous triad (hypertension, seizure, and thrombocytopenia) as a risk factor for death caused by eclampsia.

Of the limitations of this review, selection bias is the major one. In the author's opinion most deaths associated with eclampsia and pre-eclampsia during the study period were not analyzed due to the strict inclusion criteria. However, 9 studies with more than 10 deaths adhered to the strict criteria. Furthermore, few studies analyzed more than 300 maternal deaths caused by pregnancy-related hypertensive disorders. A second limitation is that relevant studies may have been missed. Medline was searched using a strategy that included MeSH terms based on key words in the relevant studies. The reference lists of the included papers were also reviewed. Another limitation is that there was no information on the number of women with HE/EH who survived, and it is not possible to ascertain this in a systematic review of mortality. Another possible limitation is the publication language of the literature selected. This review only considers studies published in 3 languages, but did not find any differences in the results when publication language was analyzed. A final possible limitation is that the review was carried out by one author. However, the search strategy was extensive, comprehensive, and reproducible.

Large prospective studies are necessary to evaluate the risk of adverse maternal outcomes in HELLP syndrome with eclampsia, or eclampsia with HELLP syndrome (HE/EH). Furthermore, it is necessary to evaluate the risk of one or multiple seizures in this group of patients. Another interesting question is whether prophylactic magnesium sulfate has any impact on maternal morbidity and mortality in women with HELLP syndrome.

In summary, eclampsia continues to be a dangerous complication of pregnancy with a high case fatality rate, and HELLP syndrome seems to be a major feature of catastrophic eclampsia.

References

- [1] Langer A, Villar J, Tell K, Kim T, Kennedy S. Reducing eclampsia-related deaths—a call to action. *Lancet* 2008;371(9614):705–6.
- [2] Katz V, Farmer R, Kuller JA. Preeclampsia into eclampsia: Toward a new paradigm. *Am J Obstet Gynecol* 2000;182(6):1389–96.
- [3] Zwart JJ, Richters JM, Öry F, de Vries JI, Bloemenkamp KW, van Roosmalen J. Severe maternal morbidity during pregnancy, delivery and puerperium in the Netherlands: a nationwide population-based study of 371 000 pregnancies. *BJOG* 2008;115(7):842–50.
- [4] Igbere GO, Ebeigbe PN. Eclampsia: ten-years of experience in a rural tertiary hospital in the Niger delta, Nigeria. *J Obstet Gynecol* 2006;26(5):414–7.
- [5] Hussain F, Johanson RB, Jones P. One year survey of maternal mortality associated with eclampsia in Dhaka Medical College Hospital. *J Obstet Gynaecol* 2000;20(3):239–41.
- [6] Isler CM, Rinehart BK, Terrone DA, Martin RW, Magann EF, Martin Jr JN. Maternal mortality associated with HELLP (hemolysis, elevated liver enzymes, and low platelets) syndrome. *Am J Obstet Gynecol* 1999;181(4):924–8.
- [7] Haddad B, Baton JR, Livingston JC, Chahine R, Sibai B. Risk factors for adverse maternal outcomes among women with HELLP (hemolysis, elevated liver enzymes, and low platelet count) syndrome. *Am J Obstet Gynecol* 2000;183(2):444–8.
- [8] Osmanagaoglu MA, Osmanagaoglu S, Ulusoy H, Bozkaya H. Maternal outcome in HELLP syndrome requiring intensive care management in a Turkish hospital. *Sao Paulo Med J* 2006;124(2):85–8.
- [9] Mattar F, Sibai B. Eclampsia. VIII. Risk factors for maternal morbidity. *Am J Obstet Gynecol* 2000;182(2):307–12.
- [10] Martin Jr JN, Rinehart BK, May WL, Magann EF, Terrone DA, Blake PG. The spectrum of severe pre-eclampsia: Comparative analysis by HELLP (hemolysis, elevated liver enzyme levels, and low platelet count) syndrome classification. *Am J Obstet Gynecol* 1999;180(6 Pt 1):1373–84.
- [11] Cavkaytar S, Ugurlu EN, Karaer A, Tapisiz OL, Danisman N. Are clinical symptoms more predictive than laboratory parameters for adverse maternal outcome in HELLP syndrome? *Acta Obstet Gynecol* 2007;86(6):648–51.
- [12] Vigil-de Gracia PE, Tenorio-Marañón R, Cejudo-Carranza E, Helguera-Martínez A, García-Cáceres E. Differences between pre-eclampsia, HELLP syndrome and eclampsia. Maternal evaluation [in Spanish]. *Ginecol Obstet Mex* 1996;64: 377–82.
- [13] Helguera-Martínez AM, Tenorio-Marañón R, Vigil-De Gracia PE, García-Cáceres E. HELLP syndrome, Analysis of 102 cases [in Spanish]. *Ginecol Obstet Mex* 1996;64:528–33.
- [14] Vigil-De Gracia P, García-Cáceres. Dexamethasone in the post-partum treatment of HELLP syndrome. *Int J Gynecol Obstet* 1997;59(3):217–21.
- [15] Vigil-De Gracia P. Maternal mortality in Panamá city (CHMCCS), 1992–1996. *Int J Gynecol Obstet* 1998;61(3):283–4.
- [16] Conde-Agudelo A, Kafury-Goeta AC. Epidemiology of eclampsia in Colombia. *Int J Gynecol Obstet* 1998;61(1):1–8.
- [17] Wijesinghe PS, Gunasekera PC, Sirisena J. Spontaneous hepatic rupture in pregnancy. *Ceylon Med J* 1998;43(2):109–11.
- [18] Onrust S, Santema JG, Aarnoudse JG. Pre-eclampsia and the HELLP syndrome still cause maternal mortality in the Netherlands and other developed countries; can we reduce it? *Eur J Obstet Gynecol Rep Biol* 1999;82(1):41–6.
- [19] Sheikh RA, Yasmeen S, Pauly MP, Kiegl J. Spontaneous intrahepatic hemorrhage and hepatic rupture in the HELLP syndrome: four cases and a review. *J Clin Gastroenterol* 1999;28(4):323–8.
- [20] Lara AL, García A, Macías E. Maternal mortality by eclampsia. Five years review [in Spanish]. *Ginecol Obstet Mex* 1999;67:253–7.
- [21] Reck T, Bussenius-Kammerer M, Ott R, Müller V, Beinder E, Hohenberger W. Surgical treatment of HELLP syndrome-associated liver rupture -- an update. *Eur J Obstet Gynecol Rep Biol* 2001;99(1):57–65.
- [22] Romero-Arauz JF, Lara AL, Ramos JC, Izquierdo JC. Maternal morbidity and mortality in HELLP syndrome [in Spanish]. *Ginecol Obstet Mex* 2001;69:189–93.
- [23] Tank PD, Nadanwar YS, Mayadeo NM. Outcome of pregnancy with severe liver disease. *Int J Gynecol Obstet* 2002;76(1):27–31.
- [24] Vigil-De Gracia P. Pregnancy complicated by pre-eclampsia-eclampsia with HELLP syndrome. *Int J Gynecol Obstet* 2001;72(1):17–23.
- [25] Soh Y, Yasuhi I, Nakayama D, Ishimaru T. A case of postpartum cerebral infarction with hemolysis, elevated liver enzymes, low platelets (HELLP) syndrome. *Gynecol Obstet Invest* 2002;53(4):240–2.
- [26] Vigil-De Gracia P, Reyes W, Rodríguez-Morales F, Cruz-Breucop R. Eclampsia in Central America [in Spanish]. *Ginecol Obstet Mex* 2002;70:545–50.
- [27] Juárez-Azpilcueta A, Motta-Martínez E, Montaña-Uzcanga A. Hepatic rupture as a complication of hypertensive disease of pregnancy and the HELLP syndrome [in Spanish]. *Gac Med Mex* 2003;139:276–80.
- [28] Ding DC, Chu TW, Liu JY. Maternal death associated with Eisenmenger's syndrome complicated with HELLP syndrome. *Int J Gynecol Obstet* 2003;83(2):189–91.
- [29] Knopp U, Kehler U, Rickmann H, Arnold H, Gliemroth J. Cerebral haemodynamic pathologies in HELLP syndrome. *Clin Neurol Neurosurg* 2003;105(4):256–61.
- [30] Capellino MF, Galetto S, Sad Larcher JM Travella C, Ferreyra M, Ruiz Orrico G. Nine cases of HELLP syndrome (hemolysis, elevated liver enzymes and low platelets) [in Spanish]. *Medicina (B Aires)* 2003;63(5):383–7.
- [31] Rodríguez AB, Pérez CP, Rocha RL, Martínez JM, Martínez A, Hernández-Valencia M. Maternal and perinatal surgical complications in low platelet count for HELLP syndrome in severe pre-eclampsia-eclampsia in intensive care unit [in Spanish]. *Ginecol Obstet Mex* 2003;71:379–86.
- [32] Agarwal U, Dahiya P, Sangwan K. Recent onset neurofibromatosis complicating eclampsia with maternal death: a case report. *Arch Gynecol Obstet* 2003;268(3):241–2.
- [33] Chen CY, Kwek K, Tan KH, Yeo GS. Our experience with eclampsia in Singapore. *Singap Med J* 2003;44(2):88–93.
- [34] Coelho TM, Martins MG, Viana E, Mesquita MR, Camano L, Sass N. Proteinuria in hypertensive syndrome of pregnancy: maternal and perinatal outcome [in Portuguese]. *Rev Assoc Med Bras* 2004;50(2):207–13.
- [35] Oettle C, Hall D, Roux A, Grove D. Early onset severe pre-eclampsia: expectant management at a secondary hospital in close association with a tertiary institution. *BJOG* 2005;112(1):84–8.
- [36] Nunes JO, Turner MA, Fulcher AS. Abdominal imaging features of HELLP syndrome: A 10-year retrospective review. *AJR Am J Roentgenol* 2005;185(5):1205–10.
- [37] Zeidman LA, Videnovic A, Bernstein LP, Pellar CA. Lethal pontine hemorrhage in postpartum syndrome of hemolysis, elevated liver enzyme levels, and low platelet count. *Arch Neurol* 2005;62(7):1150–3.
- [38] Yücesoy G, Özkan S, Bodur H. Maternal and perinatal outcome in pregnancies complicated with hypertensive disorder of pregnancy: a seven year experience of a tertiary care center. *Arch Gynecol Obstet* 2005;273(1):43–9.
- [39] Fonseca JE, Méndez F, Cataño 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):1591–8.
- [40] Demir CS, Evruke C, Ozgunen FT, Urunsak IF, Candan E, Kadayifci O. Factors that influence morbidity and mortality in severe pre-eclampsia, eclampsia and

- hemolysis, elevated liver enzymes and low platelet count syndrome. *Saudi Med J* 2006;27(7):1015–8.
- [41] van Runnard Heimel PJ, Huisjes AJ, Franx A, Koopman C, Bots ML, Bruinse HW. A randomized placebo-controlled trial of prolonged prednisolone administration to patients with HELLP syndrome remote from term. *Eur J Obstet Gynecol Rep Biol* 2006;128(1-2):187–93.
- [42] Araujo AC, Leao M, Nobrega PF, Bezerra MH, Pereira FV, Dantas EM, et al. Characteristics and treatment of hepatic rupture caused by HELLP syndrome. *Am J Obstet Gynecol* 2006;195(1):129–33.
- [43] Gaugler-Senden IP, Huijssoon AG, Visser W, Steegers EA, de Groot CJ. Maternal and perinatal outcome of preeclampsia with an onset before 24 weeks' gestation. Audit in a tertiary referral center. *Eur J Obstet Gynecol Rep Biol* 2006;128(1-2):216–21.
- [44] Minkauskiene M, Nadisauskiene RJ, Padaiga Z. Severe and acute maternal morbidity: Lithuanian experience and review. *Int J Fertil Womens Med* 2006;51(1):39–46.
- [45] Dissanayake VH, Samarasinghe HD, Morgan L, Jayasekara RW, Seneviratne HR, Pipkin FB. Morbidity and mortality associated with pre-eclampsia at two tertiary care hospitals in Sri Lanka. *J Obstet Gynaecol Res* 2007;33(1):56–62.
- [46] Chhabra S, Kakani A. Maternal mortality due to eclamptic and non-eclamptic hypertensive disorders: A challenge. *J Obstet Gynaecol* 2007;27(1):25–9.
- [47] Gómez-Puerta JA, Cervera R, Espinosa G, Asherson RA, García-Carrasco M, da Costa IP, et al. Catastrophic antiphospholipid syndrome during pregnancy and puerperium: maternal and fetal characteristics of 15 cases. *Ann Rheum Dis* 2007;66(6):740–6.
- [48] Efetie ER, Okafor UV. Maternal outcome in eclamptic patients in Abuja, Nigeria -- a 5 year review. *Niger J Clin Pract* 2007;10(4):309–13.
- [49] Miguil M, Chekairi A. Eclampsia, study of 342 cases. *Hypertens Pregnancy* 2008;27(2):103–11.
- [50] Katz L, de Amorin MM, Figueiroa JN, Pinto e Silva JL. 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–e8.
- [51] Vigil-De Gracia P, García-Cáceres E. Thrombocytopenia, hypertension and seizures in eclampsia. *Int J Gynecol Obstet* 1998;61(1):15–20.
- [52] Schutte JM, Schuitemaker NW, van Roosmalen J, Steegers EA. Substandard care in maternal mortality due to hypertensive disease in pregnancy in the Netherlands. *BJOG* 2008;115(6):732–6.
- [53] Altman D, Carroli G, Duley L, Farrell B, Moodley J, Neilson J, et al. Do women with pre-eclampsia, and their babies, benefit from magnesium sulphate? The Magpie Trial: a randomized placebo-controlled trial. *Lancet* 2002;359(9321):1877–90.
- [54] Moodley J. Maternal deaths associated with hypertension disorders of pregnancy: a population-based study. *Hypertens Pregnancy* 2004;23(3):247–56.
- [55] Mackay AP, Berg CJ, Atrash HK. Pregnancy-related mortality from preeclampsia and eclampsia. *Obstet Gynecol* 2001;97(4):533–8.
- [56] Lewis G, editor. *The Confidential Enquiry into Maternal and Child Health (CEMACH). Saving Mothers' Lives: reviewing maternal deaths to make motherhood safer 2003–2005. The Seventh Report on Confidential Enquiries into Maternal Deaths in the United Kingdom.* London: CEMACH; 2007.
- [57] Berg CJ, Chang J, Callaghan WM, Whitehead SJ. Pregnancy-related mortality in the United States, 1991–1997. *Obstet Gynecol* 2003;101(2):289–96.
- [58] Zeeman GG, Fleckenstein JL, Twickler DM, Cunningham FG. Cerebral infarction in eclampsia. *Am J Obstet Gynecol* 2004;190(3):714–20.
- [59] Martin Jr JN, Thigpen BD, Moore RC, Cushman J, May W. Stroke and severe preeclampsia and eclampsia: a paradigm shift focusing on systolic blood pressure. *Obstet Gynecol* 2005;105(2):246–54.