

Pattern of HELLP Syndrome in the Context of Severe Pre-Eclampsia in Cameroonian Hospital Environment

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ABSTRACT

Background: HELLP syndrome is a serious gravido-puerperal complication of preeclampsia. Moreover, it is associated with significant maternal and perinatal morbidity and mortality, such as blood transfusion, which were 8 times higher in patients with HELLP syndrome than in isolated PES and thus most often requiring immediate termination of the pregnancy. We therefore conducted a study on the factors associated with HELLP (Hemolysis Elevated Liver Enzymes and Low Platelets count) syndrome [SH] in patients with severe pre-eclampsia in three (03) hospitals in Yaoundé.

Methodology: We conducted a case-control study of women admitted with severe pre-eclampsia who had or had not developed HELLP syndrome; during a period from May 2019 to May 2021 in three (3) 2nd category hospitals in Yaoundé. The sampling was consecutive and not exhaustive. We included patients with a complete medical record. Statistical analysis was done using the S.P.S.S.23.0 software. The significance level was set at 0.05.

Results: A total of 19 cases of HELLP syndrome were recruited and matched to 60 controls during the study period, i.e. 1 case for every 3 controls. The univariate analysis identified the following as factors favoring HELLP syndrome The univariate analysis identified the following factors as favouring HELLP syndrome: age group [15-20 years], follow-up in a health centre, antenatal visits by nurses and epigastralgia. And as a protective factor calcium supplementation. After multivariate analysis multivariate analysis, calcium supplementation was protective against HELLP syndrome OR=0.20 IC95% (0.05-0.81) p= 0.025. In addition, having a nurse as a provider of antenatal visits was significantly associated with the occurrence of HELLP syndrome, OR=5.37; IC95% (1.37-20.44).

Conclusion: Maternal and fetal mortality associated with severe forms of pre-eclampsia remains high, hence the need for continuous improvement in its management. Calcium supplementation during pregnancy has significantly limited the occurrence of severe forms such as HELLP syndrome.

Keywords: HELLP syndrome; Factors; Severe pre-eclampsia; Yaoundé

INTRODUCTION

Hypertension and its complications are the leading causes of maternal morbidity and mortality. They are constantly increasing. One of its severe form is the HELLP (Hemolysis Elevated Liver Enzymes and Low Platelets count) syndrome [SH]. The prevalence of HELLP syndrome (SH) in the general population

varies according to the studies. Halle and Ekane found 12.6% of HELLP syndrome in patients with severe preeclampsia [1]. HELLP syndrome is associated with significant maternal and perinatal morbidity and mortality. severe anemia and acute renal failure are more important in patients with HELLP syndrome than in women with only severe preeclampsia [2,3]. Similarly, prematurity, hypotrophy and mortality were higher in newborns with mothers

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Received: 09 Mar 2022, Manuscript No. GOOCR-22-15897, Editor assigned: 11-Mar-2022, PreQC No. GOOCR-22-15897(PQ); Reviewed: 18-Mar-2022, QC No. GOOCR-22-15897; Revised: 21-Mar-2022, Manuscript No. GOOCR-22-15897(R); Published: 29-Mar-2022, DOI: 10.35248/2161-0932.22.12.589

Citation: Felix E, Junie M, Esther J, Etienne B, Xavier N, Wilfried L, et al. (2021) Pattern of HELLP Syndrome in the Context of Severe Pre-Eclampsia in Cameroonian Hospital Environment. Gyno & Obstet. 12.589.

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whom had HELLP syndrome [4,5]. Few studies have been done on HELLP syndrome in our context, and our objective was to identify the factors associated with HELLP syndrome in patients with severe preeclampsia with the aim improving reliable strategies for the prevention of severe forms of preeclampsia.

METHODOLOGY

We conducted a case-control study on women admitted for HELLP syndrome with severe preeclampsia compared to women in the control group with severe preeclampsia without HELLP syndrome. This study took place in 03 university teaching hospitals from the period from May 2019 to May 2021 comparing two groups of patients. The "case group" consisted of all patients with severe preeclampsia who presented with HELLP syndrome defined according to the Sibai criteria since 1990. All patients with thrombocytopenia, elevated LDH or AST due to other causes and incomplete records were excluded from this group. The "control group" was composed of patients with severe preeclampsia defined according to WHO and International Society for the Study of Pregnancy Hypertension

criteria by a blood pressure greater than 160/110 mmHg after 20 weeks of pregnancy, associated with significant proteinuria. This latter group was constituted on the basis of a 3:1 ratio and, this, by selecting three consecutive severe preeclampsia on controls group at each hospitalization of HELLP syndrome cases. Risk factors for HELLP syndrome were investigated by comparing sociodemographic, obstetric, clinical, and biological variables collected from both groups. The odds ratio was used to measure the association between HELLP syndrome and risk factors, with the comparison of categorical variables performed by the χ^2 test and the 95% confidence interval around it. The significance level was set at 5%. Univariate analysis was performed to determine the relationship between single risk factor and the occurrence of HELLP syndrome. Differences were considered statistically significant with $p < 0.05$. Subsequently a multivariate analysis by logistic regression to control for confounders was performed. Statistical analysis was done using the S.P.S.S.23.0 software and the significance level was set at 0.05.

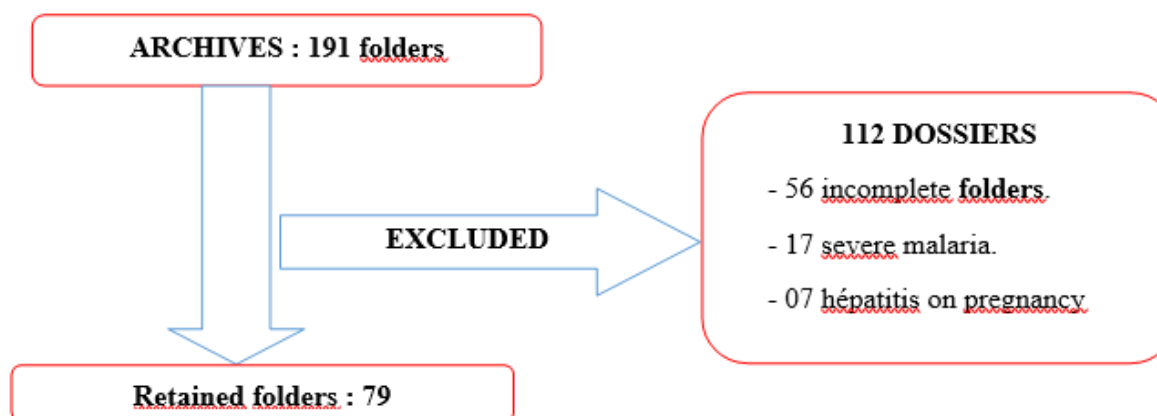


Figure 1: Flow chart of HELLP syndrome with severe preeclampsia for 60 controls of severe preeclampsia without HELLP syndrome.

Table 1: Association between socio-demographic factors and the occurrence of HELLP syndrome.

Variables	Cases n=18 (%)	Control n=61 (%)	Total N=79 (%)	OR (IC 95%)	P-value
Age					
[15-20]	9 (50,0)	14 (23,0)	23 (29,1)	3,36 (1,19-10,08)	0.001
[20-25]	1 (5,6)	9 (14,6)	10 (12,7)	0,34 (0,04-2,88)	0.279
[25-30]	3 (16,3)	14 (23,0)	17 (21,5)	0,67 (0,17-2,66)	0.417
[30-35]	2 (11,1)	9 (14,6)	11 (13,9)	0,72 (0,14-3,69)	0.519
[35-40]	3 (16,3)	16 (26,2)	19 (24,1)	0,56 (0,14-2,2)	0.310
Site of ANC					
Category 1 hospital	1 (5,6)	6 (9,8)	7 (8,9)	0,54 (0,06-4,79)	0.495
Category 2 hospital	2 (11,1)	2 (3,3)	4 (5,1)	3,68 (0,48-28,25)	0.222
Category 3 hospital	1 (5,6)	8 (13,1)	9 (11,4)	0,39 (0,04-3,34)	0.342
Category 4 hospital	4 (22,2)	21 (34,4)	25 (31,6)	0,54 (0,16-1,86)	0.249
Category 5 hospital	3 (16,7)	19 (31,1)	22 (27,8)	0,44 (0,11-1,71)	0.184
Category 6 hospital	7 (38)	5 (8,2)	12 (15,2)	7,1 (1,90-26,60)	0.004
In charge of ANC					
Gynecologist	4 (22,2)	32 (52,5)	36 (45,6)	0,14 (0,02-1,14)	0.021
General practitioners	3 (16,7)	18 (29,5)	21 (26,6)	0,18 (0,02-1,47)	0.221
Nurses/midwife	11 (61,1)	11 (18,0)	22 (27,8)	8,82 (1,86-41,74)	0.001
Prophylaxy					
Aspirine	12 (66,7)	48 (78,7)	60 (75,9)	0,54 (0,17-1,72)	0.227
Calcium	8 (44,4)	49 (80,3)	57 (72,2)	0,19 (0,06-0,60)	0.005

RESULTS

During the study period, we recruited a total of 191 cases of severe preeclampsia in these three hospitals. 112 of them were excluded and we finally retained 79 cases, that is 19 cases of HELLP syndrome with severe preeclampsia for 60 controls of severe preeclampsia without HELLP syndrome (Figure 1).

The univariate analysis revealed the following parameters as factors favoring HELLP syndrome: age [15-20 years], follow-up in a health center, prenatal visits done by nurses.

And as a protective factor, calcium supplementation. After multivariate analysis, calcium supplementation was protective against HELLP syndrome OR=0.20 (IC95% :0.05-0.81) p=0.025. In addition, having a nurse as a provider of antenatal care was significantly associated with the occurrence of HELLP syndrome, OR=5.37; 95% CI (1.37-20.44) (Tables 1 and 2).

The most frequent maternal complications was anemia 72.2% in case group and 19.7% in the control group and fetal complications were hypotrophy although not significant. In addition, treatment consisted of blood transfusion which was significantly higher in patients with HELLP syndrome (Figure 2).

DISCUSSION

Calcium supplementation for the prevention of eclampsia has been recommended by the WHO since 2013, [6] in 2010 found significantly lower serum calcium levels in patients with severe pre-eclampsia compared to mild pre-eclampsia and normo-tensive patients [6]. Furthermore [7], in 2014 in a systematic review of 13 randomized trial studies showed that calcium supplementation significantly reduced the occurrence of gestational hypertension and preeclampsia although abnormally increasing the risk of HELLP syndrome but not significantly [7]. Similarly, a French

review led by [1] showed that calcium supplementation decreased the risk of preeclampsia by 64% in patients from a country with a low calcium intake, and by 30% in the number of women with hypertension during pregnancy, all populations combined. In contrast, a randomized, placebo-controlled trial in 2006 led by [8] showed that supplementation with 1.5 g of calcium/day did not prevent the occurrence of preeclampsia but significantly reduced the index of severe preeclampsia complications [8]. Low calcium levels are important to endothelial cell activation and additional calcium can reverse the activation of the endothelium induced by proinflammatory mediators while having no effect on the production of trophoblast debris [9] have shown that the presence of inflammatory markers results in the excretion of more necrotic trophoblast debris and these debris once phagocytosed by endothelial cells results in endothelial cell activation [9]. In litterature, endothelial activation is implicated in the genesis of preeclampsia. In our study we found that calcium supplementation significantly reduced the occurrence of HELLP syndrome OR=0.19, IC95% 0.06-0.60 and a p-value=0.005 this can be explained by the application of WHO preeclampsia prevention, and that calcium supplementation reduced the occurrence of HELLP syndrome in patients with severe pre-eclampsia.

Referral was the most frequent mode of admission at 89.9% in our study. Similarly, the study by [10] in 2007 in Mali found that 52.2% of women were referred [10]; and antenatal visits by non-specialized personnel and follow-up in a health center were significantly related to the occurrence of HELLP. This is consistent with the results obtained in Benin by [11] who showed that 3/4 of the patients in their study were referred and had at least one complication of pre-eclampsia [11]. This would be linked on the one hand to the fact that these three hospitals are fulfilling their role as referral centers, and on the other hand to a poor management of preeclampsia cases in the peripheral health facilities. In fact, nurses do not have adequate training in the peripheral centers where the majority of patients monitor their pregnancies. The regulation of personnel qualifications in the field of maternal health could contribute to the prevention of risks related to pathologies in pregnancy in our environment.

Also, the poor health coverage of the country in the peripheral centers would explain the high referral rates with associated severe forms of preeclampsia.

Table 2: Results of analysis after logistic regression.

VARIABLES	OR (IC 95%)	P-value
Epigastric pain	2,34 (0,57-9,51)	0.232
Calcium prophylaxy	0,20(0,05-0,81)	0.025
Catégory 6 hospital	3,65(0,79-16,83)	0.097
Nurses/midwife	5,37 (1,41-20,44)	0.014
Age 15-20	3,5 (0,86-14,48)	0.079

MATERNO-FOETAL MORBIMORTALITY IN THE POPULATION

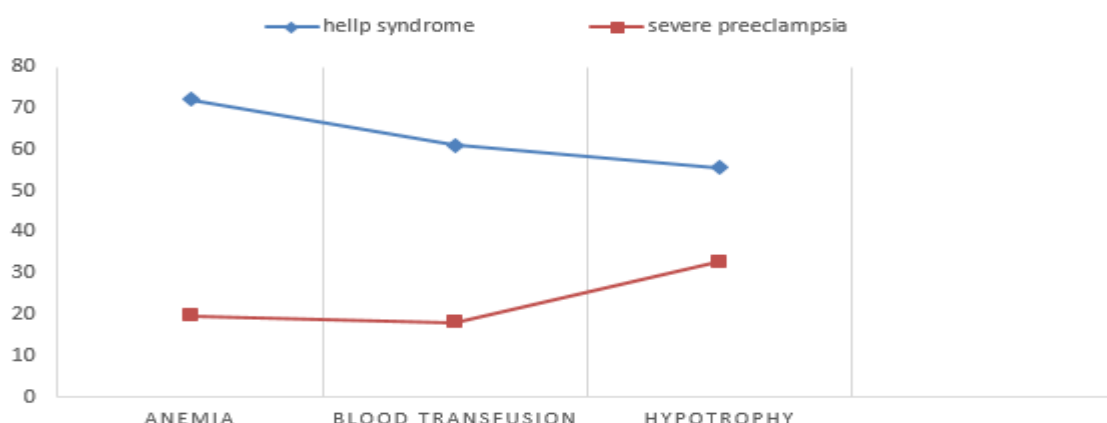


Figure 2: Complications of the HELLP syndrome.

CONCLUSION

Maternal and fetal mortality related to severe forms of preeclampsia remains high, hence there is a need for constant improvement in its management. Calcium supplementation during pregnancy has significantly limited the occurrence of severe forms such as HELLP syndrome.

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