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Severe Maternal Morbidity Associated with Early- and Late-Onset Preeclampsia

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Abstract

Background: Preeclampsia remains a leading cause of severe maternal morbidity worldwide and its early- and late-onset phenotypes are increasingly recognised as differing in severity and complication profile. This study aimed to compare the pattern of severe maternal morbidity between women with early-onset preeclampsia (EOP) and late-onset preeclampsia (LOP) and to contrast these outcomes with normotensive pregnancies. ***Methods:*** A hospital-based case control study was conducted in the Department of Obstetrics and Gynaecology, BIRDEM General Hospital, Dhaka, over six months (March to August 2019). One hundred women with preeclampsia (50 EOP and 50 LOP) and 50 normotensive controls were enrolled consecutively. Structured interview, clinical examination and review of laboratory records were used to document severe maternal complications, including HELLP syndrome, acute kidney injury (AKI) and disseminated intravascular coagulation (DIC). Data were analysed using SPSS, with the chi-square or Fisher exact test applied as appropriate and $p<0.05$ considered significant. ***Results:*** Baseline maternal age, height and weight were comparable between EOP and LOP groups ($p>0.05$). DIC occurred in 5 (10.0%) women with LOP versus none with EOP ($p=0.056$) and AKI occurred in 1 (2.0%) LOP case versus none in EOP. No maternal deaths occurred. Compared with controls, HELLP syndrome (10.0% vs 0%, $p=0.016$) and AKI (8.0% vs 0%, $p=0.034$) were significantly more frequent among women with EOP, while DIC was significantly more frequent among women with LOP than controls (10.0% vs 0%, $p=0.022$). ***Conclusion:*** Severe maternal morbidity differs qualitatively between early- and late-onset preeclampsia, with EOP more strongly associated with HELLP syndrome and acute kidney injury and LOP more strongly associated with disseminated intravascular coagulation, when each phenotype is compared with normotensive pregnancy.

Keywords: Preeclampsia; severe maternal morbidity; HELLP syndrome; acute kidney injury.

INTRODUCTION

Severe maternal morbidity, encompassing life-threatening complications such as HELLP syndrome, acute kidney injury, disseminated intravascular coagulation and eclampsia, remains one of the most serious consequences of preeclampsia and a major driver of maternal mortality in low- and middle-income countries [1,2]. Preeclampsia is estimated to complicate between 2% and 8% of pregnancies worldwide [3] and contributes to a substantial proportion of maternal deaths globally, with a disproportionate burden in resource-limited settings [1]. In Bangladesh, preeclampsia and its complications are implicated in roughly one-fifth of maternal deaths, reflecting the considerable burden of severe disease in this setting [4].

Increasing recognition that preeclampsia represents at least two distinct clinical phenotypes, early-onset preeclampsia (EOP), developing before 34 weeks

of gestation and late-onset preeclampsia (LOP), developing at or after 34 weeks, has reframed how severe maternal morbidity is understood [5]. EOP is thought to arise primarily from defective trophoblastic invasion and placental under-perfusion, producing widespread endothelial dysfunction and systemic maternal illness, whereas LOP more often reflects a relative mismatch between placental function and fetal metabolic demand in an otherwise adequately perfused placenta [6]. These differing mechanisms are believed to translate into differing patterns of severe maternal complications. A large population-based study from Washington State reported that the rate of severe maternal morbidity was more than twice as high among women with EOP as among those with LOP, with adjusted odds ratios of 3.7 and 1.7, respectively, relative to unaffected pregnancies [7]. Comparable disparities in maternal complication rates between the two phenotypes have since been reported in retrospective cohorts from low-resource hospitals in sub-Saharan Africa [8] and tertiary centers in South and Southeast Asia [9,10].

Despite this growing body of evidence, few studies have specifically examined the distribution of individual severe maternal complications, such as HELLP syndrome, acute kidney injury and disseminated intravascular coagulation, according to preeclampsia phenotype in a Bangladeshi tertiary care setting, where diagnostic and monitoring resources for early recognition of these complications may be limited. Clarifying which severe complications predominate in each phenotype has direct implications for triage, monitoring intensity and resource allocation in busy obstetric units. HELLP syndrome in particular has been most strongly linked to early-onset disease in several cohorts [11,12], whereas acute kidney injury and disseminated intravascular coagulation have shown more variable associations with onset timing depending on the population studied and the criteria used to define severe morbidity [13,14].

Given these considerations, the present study was undertaken to describe and compare the pattern of severe maternal morbidity, specifically HELLP syndrome, acute kidney injury and disseminated intravascular coagulation, between women with early- and late-onset preeclampsia attending a tertiary care hospital in Bangladesh and to contrast these complications with those observed in normotensive pregnancies, with the aim of informing phenotype-specific vigilance in antenatal and intrapartum care.

MATERIALS AND METHODS

This case control study was conducted in the Department of Obstetrics and Gynaecology, BIRDEM General Hospital, Dhaka, a tertiary referral center, over a six-month period from March to August 2019. The study population comprised pregnant women attending the inpatient and outpatient obstetric services during the study period. A total of 150 women were enrolled, including 100 women with a clinical diagnosis of preeclampsia according to American College of Obstetricians and Gynecologists criteria, subdivided into 50 women with early-onset preeclampsia (onset before 34 weeks of gestation) and 50 with late-onset preeclampsia (onset at or after 34 weeks), together with 50 normotensive pregnant women who served as controls and were admitted on the same date as the preeclamptic cases. Cases were recruited consecutively as they presented to the department and gestational age was confirmed from the last menstrual period or first-trimester ultrasonography where dating was uncertain. Women with incomplete clinical data, those unwilling to provide consent, patients who were critically ill and those younger than 15 years or older than 45 years were excluded. Data on maternal complications, including HELLP syndrome, acute kidney injury and disseminated intravascular coagulation, were collected through structured interview, clinical examination including standardised blood pressure measurement and review of relevant haematological, renal and hepatic laboratory investigation reports, using a pretested semi-structured questionnaire to ensure accuracy and consistency of data capture across participants. The study was conducted in accordance with the Declaration of Helsinki, with ethical clearance obtained from the Institutional Review Board and written informed consent secured from all participants after explanation of the study procedures, with strict confidentiality maintained through anonymised data handling. Statistical analysis was performed using SPSS software; categorical variables, expressed as frequencies and percentages, were compared between groups using the chi-square test or Fisher exact test where expected cell counts were small, given the low frequency of several severe maternal complications, while continuous baseline variables were compared using the independent samples t-test. Where an outcome did not occur in either comparison group, exact statistics could not be computed and this is indicated accordingly in the results. A p-value of less than 0.05 was considered statistically significant throughout the analysis.

RESULTS

The study included 100 women with preeclampsia, of whom 50 had EOP and 50 had LOP. Baseline maternal characteristics were broadly comparable between the two groups, as shown in Table 1. The mean maternal age was 29.0 ± 5.1 years in EOP and 28.28 ± 5.7 years in LOP (p=0.507). Mean height was 152.0 ± 6.6 cm and 152.52 ± 5.8 cm (p=0.677), respectively, while mean weight was 71.13 ± 13.9 kg in EOP and 71.58 ± 16.1 kg in LOP (p=0.881).

Table 1: Baseline maternal characteristics according to early- and late-onset preeclampsia

Characteristic	EOP (n=50)	LOP (n=50)	p-value
Age, years, mean ± SD	29.0 ± 5.1	28.28 ± 5.7	0.507
Height, cm, mean ± SD	152.0 ± 6.6	152.52 ± 5.8	0.677
Weight, kg, mean ± SD	71.13 ± 13.9	71.58 ± 16.1	0.881

Table 2 shows the distribution of severe maternal complications between the two preeclampsia phenotypes. HELLP syndrome was not documented in either group. AKI occurred in 1 (2.0%) woman with LOP and none with EOP, while DIC occurred in 5 (10.0%) women with LOP compared with none in the EOP group, although this difference did not reach statistical significance (p=0.056). No maternal death was reported in either group.

Table 2: Severe maternal complications according to preeclampsia phenotype

Maternal complication	EOP (n=50), n (%)	LOP (n=50), n (%)	p-value
HELLP syndrome	0 (0.0)	0 (0.0)	—
Acute kidney injury	0 (0.0)	1 (2.0)	1.000
DIC	0 (0.0)	5 (10.0)	0.056
Maternal death	0 (0.0)	0 (0.0)	—

Table 3 presents maternal complications among women with early-onset preeclampsia compared with normotensive controls. HELLP syndrome occurred in 5 (10.0%) women with EOP compared with none among controls (p=0.016), while AKI occurred in 4 (8.0%) women with EOP compared with none among controls (p=0.034). No case of DIC was documented among either EOP or control women in this comparison.

Table 3: Maternal complications in early-onset preeclampsia compared with normotensive controls

Outcome	Control (n=50), n (%)	EOP (n=50), n (%)	p-value
HELLP syndrome	0 (0.0)	5 (10.0)	0.016
Acute kidney injury	0 (0.0)	4 (8.0)	0.034
DIC	0 (0.0)	0 (0.0)	0.300

Table 4 presents maternal complications among women with late-onset preeclampsia compared with normotensive controls. DIC occurred in 5 (10.0%) women with LOP compared with none among controls, a statistically significant difference (p=0.022), while AKI occurred in 1 (2.0%) LOP case compared with none among controls (p=0.320). HELLP syndrome was not observed in either group.

Table 4: Maternal complications in late-onset preeclampsia compared with normotensive controls

Outcome	Control (n=50), n (%)	LOP (n=50), n (%)	p-value
HELLP syndrome	0 (0.0)	0 (0.0)	—
Acute kidney injury	0 (0.0)	1 (2.0)	0.32
DIC	0 (0.0)	5 (10.0)	0.022

DISCUSSION

In this study, women with early-onset preeclampsia (EOP) and late-onset preeclampsia (LOP) exhibited similar baseline maternal age, height and weight, indicating that the divergence in severe maternal morbidity observed between the two phenotypes cannot be attributed to differences in these baseline characteristics. This is consistent with previous comparative work by Rahman *et al.,*[9], who likewise found broadly similar demographic profiles between EOP and LOP groups despite marked differences in complication rates.

Within the preeclampsia cohort itself, disseminated intravascular coagulation occurred exclusively among women with LOP (10.0% vs 0%), although this difference did not reach conventional statistical significance (p=0.056), likely reflecting the relatively small subgroup sizes. This finding contrasts with several earlier reports in which coagulopathic complications were more frequently associated with the early-onset phenotype [7,15]; however, Sundaram [10] similarly observed that some severe complications, including abruptio placentae, could occur with comparable or even higher frequency in later-onset disease, underscoring that severe morbidity is not confined to any single phenotype and that vigilance is required across the gestational spectrum, a point also emphasised by Pettit *et al.,*[16].

When the preeclampsia subgroups were each compared against normotensive controls, a clearer phenotype-specific pattern emerged. HELLP syndrome occurred in 10.0% of women with EOP compared with none among controls (p=0.016) and acute kidney injury occurred in 8.0% of EOP cases compared with none

among controls (p=0.034), whereas neither complication was observed among women with LOP. This pattern is consistent with the pathophysiological model in which EOP arises from a more severe primary placental insult, generating greater systemic endothelial and hepatic dysfunction that predisposes to HELLP syndrome and renal injury, a mechanism supported by Ives *et al.,*[17] and by Barton and Sibai [11], who described HELLP syndrome as an expression of severe endothelial and hepatic microvascular injury most prevalent in early, more fulminant disease. Similarly, Lisonkova *et al.,*[7], in a large population-based cohort, reported adjusted odds ratios for severe maternal morbidity of 3.7 in early-onset disease compared with 1.7 in late-onset disease relative to unaffected pregnancies, a difference of similar direction, though larger in magnitude, to that observed in the present, smaller cohort.

In contrast, DIC was significantly more frequent among women with LOP than among controls (10.0% vs 0%, p=0.022), while the corresponding comparison for EOP did not reach significance. This finding may, in part, reflect the smaller absolute number of severe events available for statistical comparison within each subgroup, a limitation common to single-center studies of this size, as well as the possibility that DIC in this cohort was frequently precipitated by intrapartum events such as placental abruption or postpartum haemorrhage, which are not confined to any single onset phenotype and have been reported with comparable frequency in both EOP and LOP in other cohorts [16]. Teka *et al.,*[8], working in a similarly resource-limited tertiary hospital setting, likewise reported that although early-onset disease carried the greater overall burden of severe maternal morbidity, individual complications such as coagulopathy could occur unpredictably across both phenotypes, reinforcing the need for close monitoring irrespective of gestational age at onset.

No maternal deaths were recorded in either group in the present study, which, although reassuring, should be interpreted with caution given the relatively small sample size; larger regional audits in Bangladesh have documented maternal mortality directly attributable to preeclampsia and eclampsia at a considerably higher rate [4], underscoring that the near-miss morbidity captured here represents only part of the overall clinical burden of the disease.

Overall, these findings support the growing consensus that early- and late-onset preeclampsia differ not only in their timing but in their characteristic pattern of severe maternal complications, with EOP more strongly associated with hepatic and renal manifestations such as HELLP syndrome and acute kidney injury and LOP carrying a distinct, though not negligible, risk of coagulopathic complications such as DIC [6,18,19]. Recognising these phenotype-specific patterns can help clinicians anticipate the complications most likely to arise in each group, prioritise appropriate laboratory monitoring, such as liver function tests and platelet counts in early-onset disease and coagulation profiles in later-onset disease and allocate critical care resources more effectively in tertiary obstetric units managing high volumes of hypertensive disorders of pregnancy.

These observations are particularly relevant for tertiary referral hospitals such as BIRDEM, which manage a disproportionate share of severe obstetric complications referred from peripheral facilities with limited capacity for advanced maternal monitoring. Strengthening laboratory surveillance protocols specific to each preeclampsia phenotype, alongside clinician education regarding the differing complication profiles of early- and late-onset disease, may facilitate earlier recognition and management of severe maternal morbidity in similar low-resource obstetric settings.

Limitations and Recommendations

- Single-center design with a relatively small sample size, limiting statistical power to detect differences in infrequent complications such as DIC and acute kidney injury.
- Retrospective elements of data collection and reliance on hospital records may have introduced information bias for some maternal complications.
- The absence of maternal deaths in this cohort precludes assessment of mortality-specific differences between phenotypes.
- Findings from a single tertiary hospital may not be generalisable to primary and secondary care settings with different referral patterns.

CONCLUSION

Severe maternal morbidity differs in pattern between early- and late-onset preeclampsia. Compared with normotensive pregnancy, early-onset disease was significantly associated with HELLP syndrome and acute kidney injury, while late-onset disease was significantly associated with disseminated intravascular coagulation. No maternal deaths occurred in either group. These findings suggest that clinicians should maintain phenotype-specific vigilance, prioritising hepatic and renal monitoring in early-onset preeclampsia and coagulation surveillance in late-onset disease, to enable timely recognition and management of severe maternal complications in tertiary care settings.

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