# Missed opportunity for aspirin prophylaxis for preeclampsia prevention: a cross-sectional study from Sub-Saharan Africa

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**BACKGROUND:** Recent studies showed that aspirin for preeclampsia prevention is underused despite its effectiveness in preventing preeclampsia among patients with moderate and high risk factors. Little is known about this issue in the Sub-Saharan setting, including Ethiopia.
**OBJECTIVE:** This study aimed to determine the missed opportunity for aspirin prophylaxis among candidates for this preeclampsia preventive intervention at a national tertiary referral hospital in Ethiopia.
**STUDY DESIGN:** This was a cross-sectional study on pregnant women who had preeclampsia and who were managed at the St. Paul's Hospital Millennium Medical College (Ethiopia) over a 6-month period (April 1—September 30, 2023). Data were collected prospectively using a structured questionnaire. The primary outcome was the proportion of women who had an indication for aspirin prophylaxis for preeclampsia prevention but were not given the opportunity (missed opportunity for aspirin) among all pregnant preeclampsia patients presenting to our hospital. Secondary outcomes were adverse maternal and perinatal outcomes. Data were analyzed using SPSS version 23. Descriptive statistics were employed to analyze the data. Proportions and percentages were used to present the results.
**RESULTS:** A total of 427 pregnant women with preeclampsia were screened for inclusion and 32 of them were excluded based on the study criteria. Among the 395 pregnant women with preeclampsia who were included in the final analysis, 195 (50.6%) had an indication for aspirin prophylaxis for the prevention of preeclampsia. The mean systolic and diastolic blood pressure measurements at presentation were 153.8±12.8 and 100.6±8.5 mm Hg, respectively. Most patients had proteinuria (51.7% of the participants had a urine test-strip protein level of +2, whereas 18.5% [74/395] had a urine test-strip protein level of +1 and 10.9% had 24-hour urine protein levels in the preeclampsia range). Among the women who had an indication for aspirin prophylaxis, only 1.1% received aspirin (the missed opportunity for aspirin prophylaxis for preeclampsia prevention was 98.9%). The perinatal morality rate was 11.9%, whereas the neonatal intensive care unit admission rate was 20.5%. The rate of a low Apgar score at 5 minutes was 8.9%. Eight mothers (2.1%) developed hemolysis, elevated liver enzymes, and low platelet count syndrome, whereas another 3 (0.8%) mothers developed a pulmonary edema.
**CONCLUSION:** In this study, the missed opportunity for administration of aspirin prophylaxis for the prevention of preeclampsia was high although more than half of the study subjects were candidates for this preventive intervention. Preeclampsia was also associated with higher rates of adverse perinatal outcomes and serious maternal morbidity.

**Key words:** ASA, ASA prophylaxis, maternal mortality, preeclampsia in Ethiopia, preeclampsia missed opportunity

## Introduction

Preeclampsia (PE) typically affects 2% to 5% of pregnant women. Worldwide, it accounts for approximately 14% of all maternal deaths, and 500,000 babies die each year as a consequence of this disorder.[1,2] Although there are no representative community-based data on the magnitude of PE in Ethiopia, a recent systematic review and meta-analysis showed a pooled prevalence of 6.8% for hypertensive disorders of pregnancy.[3] The relative contribution of eclampsia to maternal deaths in hospital studies in Ethiopia has progressively increased from 6.5% in 1983 to 35.7% in 2008,[4] and currently, it is the second most common cause of maternal mortality. This is despite a significant decrease in the maternal mortality ratio in the country, from 676 per 1000 live births in 2011 to 267 per 1000 live births in 2020.[5,6] In the 2016 national survey, PE was the third leading cause

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Written informed consent was obtained from the patients.

A formal ethical clearance letter was obtained from the institutional review board of St. Paul Hospital Millennium.

All data generated or analyzed during this study are included in this published article.

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### Why was this study conducted?

Current evidence shows that preeclampsia can be prevented through appropriate screening, followed by aspirin (ASA) prophylaxis for pregnant women at moderate or high risk for preeclampsia. However, there are no data on how much this opportunity has been missed in low-income settings. This study sought to determine the missed opportunity for ASA prophylaxis among pregnant women with preeclampsia.

### Key findings

Among 395 pregnant women with preeclampsia included in this study, 195 (50.6%) had an indication for ASA prophylaxis for the prevention of preeclampsia. ASA prophylaxis was used in only 1.1% of patients (the missed opportunity for ASA prophylaxis for preeclampsia prevention was 98.9%) who had an indication for ASA prophylaxis. Preeclampsia-related perinatal complications and serious maternal morbidity rates were high.

### What does this add to what is known?

The missed opportunity for administration of ASA prophylaxis for the prevention of preeclampsia was high although more than half of the study subjects were candidates for this preventive intervention.

of death, accounting for 11% of all direct maternal deaths.[7]

The World Health Organization recommends aspirin (ASA) prophylaxis only to women at moderate or high risk for PE. Women are regarded as being at moderate risk for developing PE if they have any 2 of the following risk factors: primiparity, family history of PE, older than 40 years, or multiple pregnancy; and they are considered as being at high risk for developing PW if they have 1 or more of the following risk factors: diabetes, chronic or gestational hypertension, renal disease, autoimmune disease, positive uterine artery Doppler, history of PE, or previous fetal or neonatal death associated with PE.[8,9] Similarly, the International Federation of Gynaecology and Obstetrics 2019 pragmatic guidelines for the prevention and prediction of PE recommend that women who are identified as being at high risk should receive ASA prophylaxis that commence at 11 to 14+6 weeks of gestation at a dose of ~150 mg that should be taken every night until 36 weeks of gestation, when delivery occurs, or when PE is diagnosed.[2] Despite these strong recommendations, there are challenges to the effective implementation of ASA prophylaxis that may be related to policy, health facility, and healthcare provider and community level factors. In the United States, studies show inconsistent implementation of this recommendation.[10] The rate of aspirin use was as low as 22% among women with chronic medical illnesses who were candidates for ASA prophylaxis.[11]

The most important conditions for the implementation of ASA prophylaxis for PE in clinical settings were safety, effectiveness, and the possibility to make a well-informed autonomous decision.[12] In a study done in the Netherlands, the most reported reasons for non- or incomplete use were unawareness of ASA as a preventive intervention, concerns about potential adverse effects, and doubts regarding the benefits.[13] A recent, nationwide, mixed-method study of midwives in the United Kingdom found that 37.5% of midwives indicated inadequate engagement in conversations with women about ASA prophylaxis. The domains of knowledge (odds ratio [OR], 13.7; 95% confidence interval [CI], 5.7−32.7), professional role and identity (OR, 15.3; 95% CI, 6.4−36.7), and beliefs about capabilities (OR, 13.6; 95% CI, 6.1−30.6) were significantly associated with effective engagement.[14] Another qualitative study found that nonadherence by women was a barrier to ASA prophylaxis use for the prevention of PE and that a combination of inadequate knowledge, a lack of identification with the risk factors, and beliefs about consequences of taking medication were among the main reasons for nonadherence.[13]

Although uptake of ASA prophylaxis among candidate pregnant women is well studied in the developed world, little is known about this topic in low-income countries, such sub-Saharan Africa including Ethiopia. Understanding the missed opportunity for ASA prophylaxis among candidate pregnant women (women who have an indication for ASA prophylaxis for PE but did not take it) is essential because it will inform policy change on the prevention of PE in most of the countries in this region.

In Ethiopia, to date, there are no national guidelines on the prediction and prevention of PE. There also are no data on the use of ASA prophylaxis for PE prevention at a country level. St. Paul's Hospital Millennium Medical College is one of the leading national referral hospitals in Ethiopia. Based on clinical observation, a significant proportion of patients with PE who are managed at this hospital are believed to be candidates for the prevention of PE with ASA supplementation. Our study aimed to determine the missed opportunity for PE prevention in this tertiary setting in Ethiopia.

## Methods and Materials

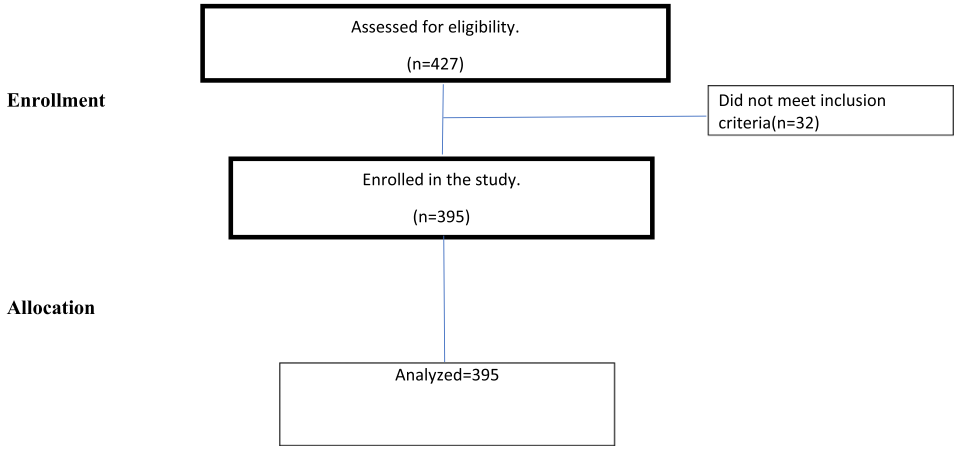
### Study design, setting, and period

We conducted a cross-sectional study on pregnant women with PE who received obstetrical care at the St. Paul's Hospital Millennium Medical College over 6 months (April 1− September 30, 2023). Data were collected prospectively. The primary outcome of our study was to determine the missed opportunity for ASA prophylaxis among patients with PE who were managed at our hospital during the study period.

### Participants

We approached pregnant women diagnosed with PE who presented for

**FIGURE**
**CONSORT flow chart**




*CONSORT*, Consolidated Standards of Reporting Trials.

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maternity care at the study hospital, St. Paul's Hospital. The inclusion criteria were pregnant women with a diagnosis of PE, irrespective of the gestational age, who delivered at our hospital and for whom the perinatal and maternal outcomes were known; singleton and higher order pregnancies; and those who volunteered to participate in the study. The exclusion criteria were postpartum PE, those who had PE but who delivered at a different hospital, those with incomplete data, and those with atypical PE.

**TABLE 1**
**Demographic and obstetric characteristics of preeclampsia patients at national tertiary referral hospital in Ethiopia, 2023**

| Variables | Category | n | Percent (%) |
|---|---|---|---|
| Maternal age (y) | Mean | 27.2 (±5.2) | |
| | ≤19 | 8 | 2.0 |
| | 20–39 | 379 | 95.9 |
| | ≥40 | 8 | 2.0 |
| Gravidity | Primigravida | 156 | 39.5 |
| | Multigravida | 239 | 60.5 |
| Previous history of abortion | Yes | 304 | 77.0 |
| | No | 91 | 23.0 |
| Gestational age (wk) | Unknown | 73 | 18.5 |
| | ≥28<34 | 38 | 9.1 |
| | 34–37 | 87 | 22.0 |
| | ≥37 | 199 | 50.4 |
| ANC status | Yes | 391 | 99.0 |
| | No | 4 | 1.0 |
| Gestational age at start of ANC | Mean | 16.7 (±4.9) | |

*ANC*, antenatal care coverage.

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## Data collection and procedures

Data were collected using a structured questionnaire prepared in English, electronically using ODK. The questionnaire had 5 sections, namely sociodemographic data, clinical characteristics including obstetrical history, laboratory findings, perinatal outcomes, and maternal outcomes. Nonrandom sampling technique was used to recruit the study participants. Pregnant women with PE admitted to the labor and delivery unit were enrolled in the study according to the inclusion and exclusion criteria. Written informed consent was obtained from the study subjects. A formal ethical clearance letter was obtained from the St. Paul's Institutional Review Board (IRB).

## Outcomes

The primary outcome of this study was to determine the missed opportunity for ASA prophylaxis among patients with PE who were managed at our hospital during the study period. We defined missed opportunity for ASA prophylaxis as the proportion of pregnant women diagnosed with PE who were candidates for ASA prophylaxis but who were not provided with ASA

among all women with PE managed at our hospital during the study period. Women were regarded as being at risk for developing PE and hence had an indication for ASA prophylaxis if they had the following risk factors: primiparity, family history of PE, older than 40 years, multiple pregnancy, diabetes, chronic hypertension, renal disease, autoimmune disease, history of PE, or previous fetal or neonatal death associated with PE. The secondary outcomes were perinatal and maternal outcomes of the study subjects.

## Statistical analysis

The sample size was calculated using single population proportion estimation formula by taking a p value of 50% (because there were no studies done in this topic) with p being the proportion of women who received PE prevention measures. We considered the margin of error to be 0.05 and a confidence interval of 95%. The calculated sample size was 384 pregnant women. It was estimated that 10% would be lost to follow-up and thus the sample size was increased to 427. After excluding 32 cases that did not meet the study criteria, a total of 395 study subjects were recruited in the study (Figure). The data were analyzed using SPSS, version 23 (IBM, Chicago, IL). Simple descriptive analyses were employed. Proportions and frequency were used to present the findings.

## Role of the funding source

Apart from allocating a financial grant to support the conduct of this study, the funder (St. Paul Institute for Reproductive Health and Rights) had no input in the study design, data interpretation, review, and approval of this report. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

## Results

The mean age of the study participants was 27.2±5.2 years. More than half of the study participants were at a gestational age of ≥37 weeks. Most of them had antenatal care coverage (ANC) and the mean gestational age at first ANC visit was 16.7±4.9 weeks (Table 1).

More than half of the patients with PE (50.9%; 195/395) included in the study had an indication for ASA prophylaxis for the prevention of PE (Table 2). The missed opportunity for PE prevention through ASA prophylaxis was 98.9% (193/195). Among the presenting symptoms (Table 3), headache (42.5%; 168/395), followed by blurry of vision (26.6%; 105/395) and right upper quadrant abdominal pain (23%; 93/395) were the most common presenting complaints. The mean systolic and diastolic blood pressure measurements at presentation were 153.8±12.8 and 100.6±8.5 mm Hg, respectively. Most patients had proteinuria (Table 4). A total of 204 (51.7%) had a urine test-strip protein level of +2, whereas another 18.5% (74/395) had a urine test-strip protein level of +1. Only 10.9% (43/395) had 24-hour urine protein level that was in the PE range (≥300 mg/dL). Among all the

**TABLE 2**
**Missed opportunity for preeclampsia prevention through aspirin prophylaxis in the index pregnancy among preeclampsia patients at national tertiary referral hospital in Ethiopia, 2023**

| Indication for preeclampsia prevention | Category | n | % |
|---|---|---|---|
| Primigravida | No | 239 | 60.5 |
| | Yes | 156 | 39.5 |
| Maternal age greater ≥40 y | No | 387 | 98.0 |
| | Yes | 8 | 2.0 |
| Did the mother has history of preeclampsia in the past? | No | 374 | 94.7 |
| | Yes | 21 | 5.3 |
| Did the mother has history of hypertension before pregnancy? | No | 383 | 97.0 |
| | Yes | 12 | 3.0 |
| Did the mother have history of renal disease? | No | 388 | 98.2 |
| | Yes | 7 | 1.8 |
| Did the mother have history of diabetes? | No | 391 | 99.0 |
| | Yes | 4 | 1.0 |
| Does the mother have history of SLE? | No | 395 | 100.0 |
| | Yes | 0 | 0.0 |
| Does the mother have history of APS? | No | 394 | 99.7 |
| | Yes | 1 | 0.3 |
| Does the mother have family history of preeclampsia? | No | 392 | 99.2 |
| | Yes | 3 | 0.8 |
| Is the index pregnancy a multiple pregnancy (twin or triplet or quadruplet)? | No | 376 | 95.2 |
| | Yes | 19 | 4.8 |
| Is the pregnancy after IVF? | No | 394 | 99.7 |
| | Yes | 1 | 0.3 |
| Total number of patients who had an indication for aspirin prophylaxis | No | 200 | 50.6 |
| | Yes | 195 | 49.4 |
| Patients who had indication for aspirin but did not take it | Missed opportunity | 193 | 98.9 |

*APS*, anti-phospholipid syndrome; *IV*, in-vitro fertilization; *SLE*, systemic lupus erythematosus.

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**TABLE 3**
**Clinical and Laboratory characteristics of preeclampsia patients at national tertiary referral hospital in Ethiopia, 2023 (n=395)**

| Variables | Category | n | % |
|---|---|---|---|
| Headache | No | 227 | 57.5 |
| | Yes | 168 | 42.5 |
| Blurring of vision | No | 290 | 73.4 |
| | Yes | 105 | 26.6 |
| Right upper quadrant abdominal pain | No | 302 | 76.5 |
| | Yes | 93 | 23.5 |
| Cough | No | 388 | 98.2 |
| | Yes | 7 | 1.8 |
| Difficulty breathing (breathing too fast, trouble catching breath) | No | 393 | 99.5 |
| | Yes | 2 | 0.5 |
| Sudden swelling in leg(s) or calf(-ves) | No | 362 | 91.6 |
| | Yes | 33 | 8.4 |
| Other | No | 381 | 96.5 |
| | Yes | 14 | 3.5 |
| Duration of illness (in d) | Mean | 5.8 (±5.4) | |
| Any signs of pallor? | No | 362 | 91.6 |
| | Yes | 33 | 8.4 |
| Icteric sclera? | No | 368 | 93.2 |
| | Yes | 27 | 6.8 |
| Fetal heartbeat on auscultation with fetoscope? | Negative | 18 | 4.6 |
| | Positive | 377 | 95.4 |
| Temperature (in Celsius) | Mean | 36.7 (±0.4) | |
| Pulse rate | Mean | 92.2 (±9.5) | |
| Respiratory rate | Mean | 20.7 (±2.1) | |
| Systolic blood pressure (mm Hg) | Mean | 153.8 (±12.8) | |
| Diastolic blood pressure (mm Hg) | Mean | 100.6 (±8.5) | |
| Uterine fundal height (wk) | Mean | 35.6 (3.3) | |

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participants, 49 (7.59%) patients with PE had a complication of intrauterine growth restriction.

When it comes to the perinatal and maternal outcomes (Table 5), the perinatal morality rate was 11.9% (47 pregnancies ended with perinatal death, 16 were stillbirths, and early neonatal death occurred in 31 cases). The low 5-minute Apgar score rate was 8.9% (43/395). The neonatal intensive care unit (NICU) admission rate was 20.5% (81/395). Cesarean delivery was the most common mode of delivery with 265 women giving birth through CD, accounting for a CD rate of 67.1%. Most of the women with PE (96.9%; 369/395) had no complications. Eight mothers (2.1%) developed hemolysis, elevated liver enzymes, and low platelet count (HELLP) syndrome, whereas another 3 (0.8%) mothers developed pulmonary edema. One patient had an acute kidney injury (AKI) and another patient had uremic encephalopathy with respiratory embarrassment.

## Discussion

### Principal findings

In this study, ASA prophylaxis for the prevention of preeclampsia was underutilized although more than half of the patients with PE had an indication for ASA for the prevention of preeclampsia. PE was also associated with increased

**TABLE 4**
**Investigation results of preeclampsia patients in Ethiopia at national tertiary referral hospital in Ethiopia, 2023 (n=395)**

| Investigation | Category | n | % |
|---|---|---|---|
| Proteinuria | Urine dipstick -negative | 74 | 18.7 |
| | Urine dipstick +1 | 73 | 18.5 |
| | Urine dipstick +2 | 204 | 51.7 |
| | Preeclampsia range 24 h- urine proteinuria | 43 | 10.9 |
| | Unknown | 1 | 0.3 |
| Obstetric ultrasound Findings | Normal intrauterine pregnancy | 303 | 76.7 |
| | Intrauterine fetal death | 16 | 3.5 |
| | IUGR | 49 | 7.59 |
| | Others | 27 | 6.83 |
| Platelet | Mean | 208 (±85) | |
| Hemoglobin (Hb) or in mg/dL | Mean | 13.0 (±1.8) | |
| Hematocrit (HCT) in % | Mean | 36.9 (±5.1) | |
| SGOT | Mean | 36.14 (±62.6 | |
| SGPT | Mean | 26.7 (±43.5) | |
| LDH | Mean | 239 (±172) | |

*LDH*, Lactate dehydrogenase; *IUGR*, intra-uterine growth restriction; *SGOT*, serum glutamic-oxaloacetic transaminase; *SGPT*, serum glutamic pyruvic transferase.

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adverse perinatal and maternal outcomes.

## Results

Despite considerable progress in the understanding of the pathophysiology and the management of PE, it still remains a common complication of pregnancy and is associated with high maternal and perinatal morbidity and mortality, especially in developing countries.[15] In a maternal death review conducted at a tertiary hospital in Ethiopia, PE was the most frequent cause of maternal death.[16] Another systemic review and meta-analysis of 13 studies showed that the prevalence of perinatal and maternal mortality among pregnant women with hypertensive disorders of pregnancy (including PE) were higher than the rates reported by high- and middle-income countries.[17] In this study, more than 1 in 10 pregnancies with PE were complicated by perinatal death (the perinatal morality rate was 11.9%; 47/395). There was a high NICU admission rate; 1 in 5 deliveries (20.5%) among the patients with PE was complicated by a need for NICU admission. Although there was no maternal death, more than 2% of the women developed HELLP syndrome. A significant number of women had different complications, including 3 pulmonary edema cases and 2 AKI cases, one of which was complicated by uremic encephalopathy and metabolic acidosis.

Recent guidelines recommend prophylactic low-dose ASA for pregnant women with risk factors for PE to reduce the risk for developing PE. A total of 15 distinct risk factors are recognized, including elements of current and past medical and obstetrical history, family history, and examination findings.[18] Despite these guidelines, clinicians often do not recommend ASA.[19] Low-dose ASA remains an underused tool for preventing PE.[20] We found this to be very true in our study. Among the women who had an indication for ASA prophylaxis in this study, less than 1% were provided with ASA accordingly although more than half (195 of 395 women) of the women enrolled in this study had an indication for ASA prophylaxis. The missed opportunity for ASA in this study is much higher than reported in previous studies. A recent study done in the United States found that only 39% received an ASA prescription of 249 patients who were considered to be at risk for PE.[21]

## Clinical implications

Our findings show that the opportunity for ASA prophylaxis for the prevention of PE is heavily missed despite the fact that PE continues to contribute to a significant proportion of the maternal mortality and morbidity and adverse perinatal outcomes in Ethiopia. It provides useful information on how much the opportunity for ASA prophylaxis for PE might have been missed at a country level given that this study was conducted at one of the biggest national referral hospitals with the most advanced maternal-fetal medicine subspecialty unit in the country that accepts huge numbers of patients with PE from different regions of Ethiopia. With Ethiopia being within the Sub-Saharan region, our findings have maternal health policy implications beyond our country in the rest of this developing region as a whole.

## Research implication

Although this study demonstrates that the missed opportunity for the prevention of PE was nearly 100% (with only 1.1% of the candidates being provided with ASA), understanding the reasons behind this significant underutilization of ASA warrant further exploration with well-designed analytical studies. Moreover, women's lived experience of missing this opportunity was not explored in our study. To this end, we recommend that a qualitative research study with the aim of documenting the lived experience of those women who missed the opportunity for ASA prophylaxis should be undertaken.

**TABLE 5**
**Perinatal and Maternal outcomes of preeclampsia patients, Ethiopia 2023**

| Variables | Category | | n | % |
|---|---|---|---|---|
| Mode of delivery | Vaginal delivery | | 130 | 32.9 |
| | Caesarean section | | 265 | 67.1 |
| Number of gestations | Singleton | | 376 | 95.2 |
| | Multiple | Total | 19 | 4.8 |
| | | Twin | 18 | 94.7 |
| | | Triplet | 1 | 5.3 |
| Newborn sex | Male | | 193 | 48.9 |
| | Female | | 202 | 51.1 |
| Birth outcome | Alive | | 375 | 94.9 |
| | Stillbirth | | 16 | 4.1 |
| | Early neonatal death | | 6 | 1.5 |
| Apgar score 1 min | < 7 | | 243 | 61.52 |
| | ≥ 7 | | 150 | 34.0 |
| | Not recorded | | 2 | 0.07 |
| Apgar score 5 min | < 7 | | 35 | 8.9 |
| | ≥ 7 | | 356 | 90.1 |
| | Not recorded | | 4 | 1.0 |
| NICU referral | Total referred | | 81 | 20.5 |
| | Discharged with improvement after treated in NICU | | 56 | 69.1 |
| | END | | 25 | 30.9 |
| Immediate cause of neonatal death in NICU | Respiratory failure | | 17 | 68.0 |
| | Multiorgan failure | | 5 | 20.0 |
| | Acute Respiratory Distress Syndrome | | 2 | 8.0 |
| | Intracranial hemorrhage | | 1 | 4.0 |
| Perinatal mortality | END+stillbirth | | 47 | 11.9 |
| Maternal complications | Cured and discharged with improvement | | 369 | 96.9 |
| | HELLP syndrome | | 8 | 2.1 |
| | Pulmonary edema | | 3 | 0.8 |
| | AKI | | 1 | 0.25 |
| | Uremic encephalopathy plus respiratory failure secondary to metabolic acidosis | | 1 | 0.25 |

*AKI*, acute kidney injury; *END*, early neonatal death; *HELLP*, hemolysis, elevated liver enzymes, and low platelet count; *NICU*, neonatal intensive care unit.

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## Strengths and limitation

Strengths of this study include prospective data collection and proper sample size allocation. A relatively short duration of data collection time and a lack of random sampling technique during recruitment of the study subjects are the main limitations. Adding a lived experience of patients with PE who were candidates for ASA prophylaxis in this study in a form of qualitative data could have strengthened our conclusions further.

## Conclusion

In this study, the missed opportunity for ASA prophylaxis administration for the prevention of PE was high although more than half of the study subjects were candidates for this preventive intervention. PE was also associated with a high rate of perinatal complications and serious maternal morbidity. These findings imply that the time to work on realizing the strategy for the prevention of PE proactively and effectively is now. The study results also have implications for informing PE

prevention strategy improvements beyond the study setting in Ethiopia and beyond Ethiopia considering that this setting is among the biggest maternity centers in the country. ■


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