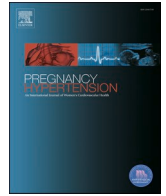




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Why magnesium sulfate ‘coverage’ only is not enough to reduce eclampsia: Lessons learned in a middle-income country

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ABSTRACT

Objectives: Determine the eclampsia prevalence and factors associated with eclampsia and recurrent seizures in Suriname and evaluate quality-of-care indicator ‘magnesium sulfate (MgSO₄) coverage’.

Study design: A two-year prospective nationwide cohort study was conducted in Suriname and included women with eclampsia at home or in a healthcare facility.

Main outcome measures: We calculated the prevalence by the number of live births obtained from vital registration. Risk factor denominator data concerned hospital births. Descriptive statistics and multivariate regression analysis were performed.

Results: Seventy-two women with eclampsia (37/10,000 live births) were identified, including two maternal deaths (case-fatality 2.8%). Nulliparity, African-descent and adolescence were associated with eclampsia. Adolescents with eclampsia had significantly lower BPs (150/100 mmHg) than adult women (168/105 mmHg). The first seizure occurred antepartum in 54% (n = 39/72), intrapartum in 19% (n = 14/72) and postpartum in 26% (n = 19/72). Recurrent seizures were observed in 60% (n = 43/72). MgSO₄ was administered to 99% (n = 69/70) of women; however 26% received no loading dosage and, in 22% of cases MgSO₄ duration was <24 h, i.e. guideline adherence existed in only 43%. MgSO₄ was ceased during CS in all women (n = 40). Stable BP was achieved before CS in 46%. The median seizure-to-delivery interval was 27 h, and ranged from four to 36 h.

Conclusion: Solely ‘MgSO₄ coverage’ is not a reliable quality-of-care indicator, as it conceals inadequate MgSO₄ dosage and timing, discontinuation during CS, stabilization before delivery, and seizure-to-delivery interval. These other quality-of-care indicators need attention from the international community in order to reduce the prevalence of eclampsia.

1. Introduction

Hypertensive disorders of pregnancy (HDP) are responsible for 14% of maternal deaths globally [1]. In Latin America and the Caribbean, HDPs are the most common causes of maternal deaths (22%) [1]. Middle-income country Suriname is known to have a high maternal

mortality ratio (MMR) (130/100,000 live births) [2] and a high rate of stillbirths (14/1,000 births) [3,4], both caused or aggravated by HDP in 30–40% of cases. Eclampsia, seizures related to HDPs, is a severe and life-threatening complication leading to significant mortality and morbidity [5,6]. The prevalence of eclampsia varies globally from 1 to 400 per 10,000 live births, with a case fatality rate of up to 10% in low-

Abbreviations: HDP, Hypertensive Disorders of Pregnancy; HELLP, Hemolysis, Elevated Liver enzymes, Low Platelets; INOSS, International Obstetric Surveillance System; LMIC, Low- and Middle-income countries; MgSO₄, Magnesium Sulfate; PE, Pre-eclampsia; SMO, Severe Maternal Outcomes; SurOSS, Suriname Obstetric Surveillance System; WHO, World Health Organization.

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income countries [7]. The Eclampsia-trial (1995) established the efficacy of magnesium sulfate (MgSO₄) in preventing recurrent seizures following eclampsia [8]. Subsequently, the Magpie-trial (1998–2001), in which 85% of recruited women were in low- and middle-income countries (LMIC), established that administration of MgSO₄ reduces the risk of death due to eclampsia by >50% [9]. Following these findings, the increasingly used MgSO₄ in high-income countries went hand in hand with a steady decrease in maternal mortality and prevalence of eclampsia [10–12].

To monitor effective interventions to reduce maternal mortality, the World Health Organization (WHO) developed the process indicator 'proportion of women with eclampsia who received MgSO₄' and defined inadequate 'coverage' as below 95% [13]. However, in a study among twenty-nine LMICs (2010–2011), mortality due to eclampsia was not reduced, despite high MgSO₄ 'coverage' [14]. Therefore, using MgSO₄ alone may not achieve the intended effect. In all likelihood, additional, more difficult to measure dimensions of quality-of-care such as prevention strategies, pre-delivery stabilization, including hypertension management and timing of childbirth, are also important [10,15,16]. These dimensions of quality-of-care need more research attention.

Suriname, a middle-income country with a small population (roughly half a million) in South America, has a well-structured health care system with the majority of deliveries by qualified birth attendants and adequate availability of essential medication [17–19]. Since 2016, the Surinamese Maternal Mortality committee consistently reviews maternal deaths [2], conducts studies on maternal near-miss [18] and stillbirths [3,4], and implemented national guidelines on HDP [17]. These activities provide the necessary infrastructure for high-quality audits of eclampsia quality-of-care. The aims of this nationwide study in Suriname were to (1) determine the nationwide prevalence of eclampsia, (2) assess factors associated with eclampsia, and (3) audit the different dimensions of quality-of-care, with particular attention to the timing and dosage of MgSO₄.

2. Methods

2.1. Study design and setting

A two-year, nationwide, prospective cohort study was conducted in Suriname between March 2017 and February 2019 [18]. Suriname is situated on the Northern coast of South-America, with a population of approximately 560,000 and 10,000 live births a year [19]. Approximately 86% of all births occur in the country's five hospitals, while 4% of women deliver at home, 6% of women deliver at the two primary health care services, and in 4%, the place of birth is unknown [19]. In general, all women with severe morbidity are referred to a hospital [18]. Maternal deaths (both those that take place in facilities and also in the community) are reported to the Surinamese Maternal Mortality Committee.

2.2. Data sources

Our previous publication elaborately described details of the data collection process [18]. Suriname Obstetric Surveillance Study (Sur-OSS), a study on severe maternal morbidity, prospectively identified all women with eclampsia by weekly screening of all discharged patients' files. The authors retrieved the data from their medical records: demographics, general and obstetric history, complications and laboratory values and management (MgSO₄ dosage, duration, and continuation during delivery, fluid charts, blood pressures (BP) at different time points, anti-hypertensive medications, time intervals between events). Additionally, an elaborate case summary was made of all cases of eclampsia (eFigure 1). The Surinamese Maternal Mortality Committee conducted verbal autopsies and maternal death reviews of each maternal death.

The number of live births were obtained from vital registration to

assess eclampsia prevalence. We used hospital deliveries (babies with a birth weight of ≥ 500 g) without eclampsia during one year (2017-03 to 2018-02) as a reference group to assess risk indicators.

2.3. Definitions, variables, and quality-of-care indicators

We defined eclampsia using the Delphi-validated International Network of Obstetric Surveillance System (INOSS) [6], as seizure(s) in a woman during pregnancy or up to 14 days postpartum, without any other attributable cause, and with at least one of the following conditions:

- Hypertension (≥ 140 mmHg systolic or ≥ 90 mmHg diastolic)
- Proteinuria (at least 1 g/l [2^{+}] on dipstick testing)
- Thrombocytopenia (platelet count of $<100 \times 10^9/L$)
- Raised plasma ALT or AST (twice the upper limit of normal) [6].

The characteristics and clinical outcomes examined for women with eclampsia included adolescent pregnancy (childbirth below the age of 20 years [20]), ethnicity (self-reported [19]), preterm delivery (before 37 weeks [21]), low birth weight (below 2500 g [21]), low Apgar score (below seven at five minutes [21]), obstetric hemorrhage (at least 500 mL blood loss during birth and in the first 24 h following birth [22]), pre-existing hypertension (BP $\geq 140/90$ mmHg, before the 20th week of pregnancy [17,23,24]) and severe hypertension (BP $\geq 160/110$ mmHg [17,23,24]) as measured by manual or automatic manometers. Eclampsia during the third stage of labor was considered 'postpartum'. A maternal near-miss, a woman who survived a life-threatening complication, had organ-dysfunction according to WHO criteria [13]. We assessed quality-of-care by using previously conducted criteria-based audits [25–27] and the Surinamese HDP guideline [17], which is based on international recommendations [23,24]:

- Aspirine prevention < 20 weeks of gestation in women with HDP during a previous pregnancy;
- Anti-hypertensive medication by oral administration in cases of BP 150/100–159/109 mmHg and intravenous administration where BP $\geq 160/110$ mmHg;
- MgSO₄ regimen loading dosage 4–6 g in 5–30 min, followed by a maintenance dosage of 1 g/hour during at least 24 h;
- MgSO₄ bolus of 2 g in 5 min in recurrent seizure(s) under MgSO₄.
- Stabilization was defined as adequate MgSO₄ therapy and BP < 160/110 mmHg before initiation of the cesarean section.

The national HDP guideline was developed in Suriname in November 2017 [17]. The guideline development process was initiated by committee Maternal Mortality Suriname (MaMS) in close collaboration with local health care providers and international experts. They compared the five hospitals' local protocols or standards of care, international indicators and recommendations and distributed the drafted guideline. During a national conference for all maternal health care professionals and policymakers, the guideline indicators and recommendations were discussed and finalized [17]. The guideline was first distributed in February 2018 and renewed in May 2019, following the second national maternal care guideline conference organized by committee MaMS.

2.4. Statistical analysis

SPSS (IBM version 25) was used for statistical analyses. The prevalence of eclampsia was calculated per 10,000 live births using the number of national live births during the study period, obtained from the Surinamese Central Bureau of Statistics. We calculated the 95% confidence interval for the prevalence and case fatality rate manually. The Mann–Whitney *U* test tested differences between continuous data. Univariate and multivariate logistic regression was performed to assess factors associated with eclampsia, reported in (adjusted) odds ratios

(OR) with 95% confidence intervals (95% CI). Multivariate analysis included the variables with p -value ≤ 0.05 in the univariate analysis. Eclampsia was the dependent variable for maternal characteristics (explanatory variables). Eclampsia was the independent variable for each adverse perinatal outcome measure (e.g., stillbirths, low Apgar score), with maternal characteristics (p -value ≥ 0.05 in univariate analysis) were the other possible explanatory variables. Missing data were $< 5\%$ and presumed to miss at random. The significance level was set at a p -value < 0.05 .

2.5. Ethical approval

The ethical review board of the Surinamese Committee on Research Involving Human Subjects (#VG21-16) approved this research on October 4, 2016. The review board required no additional approval for the analysis of anonymous medical record data.

3. Results

During the nationwide two-year prospective study period, Suriname registered 19,652 live births. Of these live births, seizures were reported in 74 women (0.38%). Two women were excluded because seizures were attributed to other causes (epilepsy and hypoglycemia). The resulting prevalence was 37 per 10,000 live births since 72 women fulfilled the eclampsia definition (95% CI 32–41 per 10,000 live births). eFigure 1 depicts all women with eclampsia in Suriname. There were two maternal deaths related to eclampsia, resulting in a case fatality rate of 2.8% (95% CI 0.8–4.7%). One of these women died during a cesarean section (CS), and the second woman, who did not receive prenatal care despite a history of eclampsia, died at home due to eclampsia.

The prevalence of eclampsia varied between the hospitals, with referral hospital I reporting the most cases, 58 per 10,000 live births, and hospital IV reporting the least number of cases, 13 per 10,000 live births. Characteristics of women with and without eclampsia are shown in Table 1, and risk indicators are demonstrated in Table 2. Nulliparity, adolescent pregnancy, and women African-descent were significantly associated with eclampsia and had two to three times the odds of eclampsia. Adverse perinatal outcomes were more likely in women with eclampsia than in women without, with aORs between 5.2 and 15.5 (95%CI between 2.5 and 36.9 after adjustment for maternal factors) (Table 2).

The clinical condition of women with eclampsia is depicted in Table 3. In women with eclampsia in Suriname, the first seizure occurred antepartum in 54% ($n = 39$), intrapartum in 19% ($n = 14$), and postpartum in 26% ($n = 19$). In 35% ($n = 25/72$) women had their first seizure at home, and in 65% ($n = 47/72$), they had their first seizure at the hospital. In 58% of cases ($n = 42/72$) HDP was diagnosed before eclampsia. Hypertension was present in 93% ($n = 65/69$, missing $n = 3$) of women with eclampsia, and severe hypertension was present in 72% ($n = 50/69$). Sixty percent ($n = 43/72$) of women with eclampsia had more than one seizure. Recurrent seizures during hospitalization were reported in 46% of women ($n = 33/71$, $n = 1$ woman died at home). Women with eclampsia met WHO near-miss criteria (i.e. organ-dysfunction) in 31% of cases ($n = 22/72$).

Of the Surinamese adolescents with eclampsia ($n = 22$), 50% ($n = 11$) had severe hypertension, 32% ($n = 7$) had mild hypertension, and 18% ($n = 4$) were normotensive (eFigure 2). In general, adolescents had a significantly lower BP before or during the seizure than adults (eFigure 3). Adolescents' median systolic BP was 150 (IQR 140–170) mmHg compared to 168 (IQR 160–180) mmHg in adults ($p = 0.041$). Their diastolic BP was 100 (IQR 90–100) mmHg compared to 105 (IQR 100–112) mmHg in adults ($p = 0.004$). The median time between a woman's first seizure and her hospital admission was two (IQR 01:21 – 03:00) hours. Women who experienced a seizure at home ($n = 18$) arrived at the hospital within one hour in 17% of cases ($n = 3$), within two hours in 50% ($n = 9$) of cases, and in more than two hours in 33% (n

Table 1

Perinatal characteristics of women with and without eclampsia.

	Eclampsia n = 72 (%)	No eclampsia ^a n = 9148 (%)	p-value
Age			
Median, IQR	23, 19–28	27, 22–32	0.002
<20 years	22 (31)	1237 (13)	
20 – 34 years	44 (61)	6549 (72)	<0.001
>35 years	6 (8)	1346 (15)	
Missings	–	227	
Parity			
Median, IQR	0, 0–1	1, 0–2	<0.001
Nullipara	46 (64)	3124 (34)	
1–3	23 (32)	4772 (52)	<0.001
≥4	3 (4)	1220 (13)	
Missings	–	32	
Ethnicity			
Hindustani	9 (12)	1733 (19)	
African-descent	51 (71)	4606 (51)	
Javanese	2 (3)	941 (10)	0.010
Mixed/other	7 (10)	1482 (16)	
Indigenous	3 (4)	347 (4)	
Missings	–	39	
Residency			
Urban	62 (88)	N/A	
Coastal	4 (6)	N/A	
Rural	4 (6)	N/A	
Missings	2		
Insurance			
None	6 (8)	N/A	
Private	20 (28)	N/A	
State	46 (64)	N/A	
Antenatal care			
Yes	59 (89)	N/A	
No	7 (11)	N/A	
Missings	6		
Multiple pregnancy			
Singleton	71 (99)	9028 (99)	0.954
Twins	1 (1)	120 (1)	
Chronic hypertension	7/71 (10)	N/A	
HDP in prior pregnancy	13/26 (50)	N/A	
Cesarean section scar	7/26 (27)	N/A	
	Eclampsia n=72 (%)	No eclampsia ^a n=9148 (%)	p-value
Gestational age at delivery			
Median, IQR	36, 33–38	39, 38–40	0.002
<34 ⁰ weeks	19 (26)	452 (5)	
34 ⁰ –36 ⁶ weeks	20 (28)	819 (9)	
≥37 ⁰ weeks	33 (46)	7846 (86)	<0.001
Missings	1	31	
Mode of delivery			
Vaginal delivery	26 (37)	7003 (77)	<0.001
Cesarean section	45 (63)	2142 (23)	
Missings	1	3	
Blood loss			
Median, IQR	200, 150–400	150, 100–250	0.001
<500 mL	54 (78)	8051 (91)	
500–999 mL	9 (13)	631 (7)	<0.001
1000–1999 mL	6 (9)	164 (2)	
Missings	3	302	
Birth weight			
Median, IQR	2380, 1600–2975	3070, 2735–3390	<0.001
<1500 g	15 (22)	279 (3)	
1500–2499 g	22 (32)	1026 (11)	<0.001
≥2500 g	32 (46)	7795 (86)	
Missings	3	48	
NICU admission			
Yes	17 (27)	N/A	
No	46 (73)	N/A	

(continued on next page)

Table 1 (continued)

	Eclampsia n=72 (%)	No eclampsia ^a n=9148 (%)	p-value
APGAR 5 min			
7 or higher	52 (84)	8742 (98)	<0.001
<7	10 (16)	159 (2)	
Missings	10	247	
Stillbirth			
Yes	9 (13)	175 (2)	<0.001
<28 weeks	2		
≥28 weeks	7		
Neonatal death			
Early (0–7 days)	1 (16)	N/A	
Late (8–28 days)	1 (16)	N/A	

^a Hospital deliveries during one year, represent approximately 86% of live births in the country. Vital statistics could not be used due to lack of national disaggregated perinatal data for all (live) births.

= 6).

Table 4 describes the audit of eclampsia quality-of-care. None of the thirteen women with HDP in their obstetric history received prophylactic aspirin before the 20th week of gestation. Women with a first seizure in the hospital received prophylactic MgSO₄ in 17% (n = 8/47) (eFigure 4). Further, all but one women with eclampsia received therapeutic MgSO₄ therapy during hospital admission (99%, n = 69/70, one maternal death at home, and one missing file). However, the loading dosage was inadequate in 26% of these women (n = 17/65, n = 7 missing, eFigure 5), and the duration was shorter than 24 h in 22% of the cases (n = 15/69, n = 3 missing, eFigure 6). Women with recurrent seizures during MgSO₄ therapy received a bolus in 25% of cases (n = 4/16, eFigure 7). Women received MgSO₄ before CS in 97% of cases (n = 39/40). However, in 21% of these cases (n = 8/39), no loading dosage was administered. Intra-operative seizures occurred in 25% (n = 10/40) of women with (pre-)eclampsia who received a CS (eFigure 8). MgSO₄ was ceased during the CS in all women (eFigure 9). Fifteen minutes prior to the CS, 53% (n = 20/37, missing n = 3) of women had a BP > 160/110 mmHg (eFigure 9 and eFigure 10). The median interval between first antepartum seizure and delivery was 27 h (eFigure 11); this ranged from four (>37 weeks) to 36 h (gestation < 34 weeks) (Table 4, eFigure 11).

Fig. 1 summarizes the problems identified during the case studies and recommendations based on the quality-of-care audits.

4. Discussion

4.1. Key findings

In this nationwide prospective surveillance study in Suriname, eclampsia prevalence was 37 per 10,000 live births (1 in 270 live births), with 60% of women experiencing recurrent seizures. Eclampsia was associated with adolescence, nulliparity, and African-descent.

Table 2

Association between maternal characteristics and eclampsia and eclampsia and perinatal outcomes, odds ratio's with 95%CI.

	Eclampsia n = 72 (100%)	No eclampsia n = 9148 (100%)	p-value	cOR [95% CI]	p-value	aOR [95% CI]
Characteristics ^a						
Nulliparous	46/72 (64%)	3124/9116 (34%)	<0.01	3.4 [2.1–5.5]	<0.01	3.0 [1.7–5.1]
African-descent	51/72 (71%)	4604/9109 (51%)	<0.01	2.4 [1.4–4.0]	<0.01	2.9 [1.7–4.9]
Adolescent	22/72 (31%)	1237/9132 (13%)	<0.01	2.8 [1.7–4.7]	0.01	2.2 [1.3–4.0]
Cesarean section	45/71 (63%)	2142/9145 (23%)	<0.01	5.3 [3.3–8.6]	<0.01	6.0 [3.6–10.1]
Obstetric hemorrhage	15/69 (22%)	795/8846 (9%)	<0.01	2.8 [1.6–5.0]	0.07	1.8 [1.0–3.2]
Perinatal outcomes ^b						
Preterm	39/71 (55%)	1271/9117 (14%)	<0.01	7.5 [4.7–12.1]	<0.01	6.8 [4.2–11.2]
Low birth weight	37/69 (54%)	1305/9100 (14%)	<0.01	6.9 [4.3–11.1]	<0.01	5.8 [3.6–9.5]
Low Apgar score	10/62 (16%)	234/8901 (3%)	<0.01	7.1 [3.6–14.2]	<0.01	5.2 [2.5–11.0]
Stillbirth	9/72 (13%)	175/9148 (2%)	<0.01	7.3 [3.6–15.0]	<0.01	15.5 [6.5–36.9]

^aEclampsia is the dependent variable; ^b Eclampsia is the independent variable, adjusted for maternal characteristics with p < 0.05 in univariate analysis.

Adolescents with eclampsia had lower median blood pressures than adults, leading to diagnostic delay or failure of pre-eclampsia and the possible sequelae of eclampsia. Practically all women with eclampsia received MgSO₄ (99%). Beyond the associations indicated above, factors that may have contributed to the high prevalence of eclampsia and recurrent seizures included suboptimal dosing, short duration of MgSO₄, and cessation of MgSO₄ during CS. Other factors included unstable BP during CS and a long seizure-to-delivery interval. Reporting the prevalence of eclampsia and 'MgSO₄ coverage' alone is not a reliable to assess quality-of-care indicator and additional indicators are necessary to develop justified recommendations for the reduction of eclampsia-related maternal and perinatal mortality.

4.2. Strengths and limitations

Our study's strength includes its prospective, nationwide population-based design and the rigorous method of data acquisition, which minimized underreporting. One of the limitations was that we did not study women with pre-eclampsia, who ultimately did not develop eclampsia. As a result, we could not address quality-of-care for women with pre-eclampsia or study which women developed eclampsia. Further, the reference group was limited to one year, and potential explanatory factors (such as socioeconomic status, body mass index, or pre-existing disease) were not available.

4.3. Other studies

A study in fourteen tertiary hospitals in six Latin American countries (2012) reported a prevalence of eclampsia of 17 per 10,000 live births [28], much lower than in Suriname. Brazilian researchers (2009–2010) reported a prevalence of 22 out of 10,000 live births in the Southeast region (a higher-income locality), while they found 83 out of 10,000 live births in the North (a lower-income region) of the country [29]. The contrast in prevalence emphasizes the persisting global inequity in access and quality-of-care for women living in different geographical environments [30]. Ethnic disparities, with African-descendants at highest risk, are seen within and between countries and are most likely a consequence of socioeconomic inequality and healthcare inequity [3,30]. Eclampsia is more common among adolescents than in other age groups [7,31–33]. The prevalence of adolescent pregnancy in women with eclampsia was 31% in Suriname, compared to 26–55% in Latin American countries [28]. A hypothesis is that the lower socioeconomic status within populations with high adolescent birth rates, such as Indigenous and African-descendant women, contribute to this higher prevalence [3,30,31]. Another hypothesis for the high proportion of adolescents with eclampsia is that young women generally have lower median BPs than older women, leading to diagnostic delay or failure of pre-eclampsia and the possible sequelae of eclampsia [32].

A Colombian study demonstrated that adolescents with eclampsia had normal BPs in almost half of the cases [33], similar to our results in

Table 3

Clinical condition of women with eclampsia.

	Eclampsia n = 72 (100%)
Time of first fit	
Antepartum	39 (54)
Intrapartum	14 (19)
Postpartum	19 (26)
Within first hour (n = 19)	7 (37)
Place of first fit	
Home ^a	25 (35)
Hospital ^b	47 (65)
Total number of fits	
One fit	29 (40)
Two fits	25 (35)
Three or more fits	18 (25)
Recurrent fit in hospital	33 (46)
Women who had first fit at home (n = 25)	10 (40)
Women who had first fit in hospital (n = 47)	23 (49)
Diagnosis of HDP/chronic HT prior to admission	12 (17)
Signs or symptoms (n = 69)	
No signs recorded	26 (38)
Headache	33 (48)
Visual disturbances	14 (20)
Abdominal tenderness	4 (6)
Hyperreflexia	3 (4)
Highest blood pressure recorded (n = 69)	
Hypertension $\geq 140/90$ mmHg	65 (94)
Severe hypertension $\geq 160/110$ mmHg	50 (72)
Systolic, median [Q1, Q3]	180 [160, 190]
≥ 160 mmHg	55 (80)
≥ 140 mmHg	63 (91)
Diastolic, median [Q1, Q3]	110 [100, 120]
≥ 110 mmHg	43 (62)
≥ 90 mmHg	64 (93)
Laboratory values (n = 70)	
Proteinuria present (≥ 0.3 g/L or dipstick 1 +) (n = 48)	37 (77)
HELLP	8 (11)
Hemoglobin lowest [Q1, Q3]	5.4 [4.7, 6.3]
Thrombocytopenia below 100	10 (14)
Elevated liver enzymes (2x normal value)	13 (19)
Creatinine elevated	3 (4)
Uric acid elevated	16 (21)
WHO maternal near-miss	22 (31)
ICU-admission	36 (50)
Any adverse outcome	22 (31)
Placental abruption	6 (9)
Pulmonary edema	3 (4)
Liver rupture	1 (1)
Cerebral vascular incident	4 (6)
Maternal deaths	2 (3)
Stillbirths	9 (13)
Neonatal deaths < 28 days after birth	2 (3)

^a First fit at home was antepartum in 92% (n = 23/25) and postpartum in 8% (n = 2/25).

^b First fit in hospital was antepartum in 36% (n = 17/47), intrapartum in 32% (n = 15/47) and postpartum in 32% (n = 15/47).

Suriname. Before 2000, International guidelines for HDP included a relative increase in BP (30 mmHg systolic and 15 mmHg diastolic) [34]. This criterion was removed, based on findings from two studies, conducted in New Zealand [35] and the USA [36], where the rise of basal BP (first BP at booking) $\geq 30/15$ mmHg in healthy nulliparous women was not associated with complicated pregnancies. However, these studies reported no cases of eclampsia and did not analyze adolescents separately. Revising diagnostic HDP criteria by including the relative increase of BP in high-risk populations at risk of underdiagnosis with absolute BP criteria (adolescents), may help reduce the prevalence and burden of eclampsia [33].

Table 4

Audit of management in women with eclampsia.

	Eclampsia n = 70 ^a (100%)
Prevention	
Aspirin prophylaxis from 12th to 36th week of pregnancy in women with history of HDP (n = 13)	0 (0)
Prophylactic MgSO ₄ in women who experienced first fit in the hospital (n = 47) (eFigure 4)	8 (17)
Management of hypertension	
Antihypertensive (oral or parenteral) medication, in women with BP > 160/110 mmHg (n = 60)	59 (98)
■ Parenteral therapy in women with BP > 160/110 mmHg (n = 59)	35 (59)
■ Parenteral therapy in women with BP > 180/120 mmHg (n = 37)	22 (59)
Therapeutic magnesium sulfate ^b (eFigure 5–7, 9)	69 (99)
Regimen according to national guideline ^b (n = 65, missing n = 7)	28 (43)
■ Loading dose 4–6 g in 5–30 min (n = 65)	48 (74)
■ Maintenance 1–2 g per hour (n = 69)	69 (100)
■ Total duration of MgSO ₄ therapy at least 24 h (n = 69)	54 (78)
■ Bolus during recurrent fit while on magnesium sulfate (n = 16)	4 (25)
■ Continuation of MgSO ₄ therapy during cesarean section (n = 40)	0 (0)
Stabilization for cesarean section in women with ante or intrapartum eclampsia (n = 40) (eFigure 9 and 10)	
Patient received MgSO ₄ before CS and had stable BP during CS (n = 37)	16 (43)
■ Blood pressure stable during CS (<160/110 mmHg) (n = 37)	17 (46)
■ Received MgSO ₄ before CS	39 (98)
Interval eclampsia and delivery, hh:mm, median [IQR] (eFigure 11)	
Antepartum (n = 39)	27:35 [15:20–40:51]
■ <34 weeks (n = 16)	36:00 [27:00–42:45]
■ 34–36 weeks (n = 15)	22:42 [17:19–48:25]
■ ≥ 37 weeks (n = 8)	3:46 [03:03–11:03]
Antepartum or intrapartum (n = 53)	16:33 [03:17–36:00]
Intrapartum (n = 14)	1:30 [00:33–02:15]
Interval > 24 h (n = 53)	20 (38)
Interval > 48 h (n = 53)	9 (17)
Other	
Benzodiazepines, total (n = 61)	27 (44)
Benzodiazepines, prior to or simultaneously with MgSO ₄ (n = 61)	21 (34)

^a One medical file could not be found and one woman died at home.

^b MgSO₄ regimen according to guideline entails loading dose of 4–6 g in 5–30 min, followed by 1 g per hour during at least 24 h and a bolus of 2 g in 5 min in recurrent fit under MgSO₄.

4.4. Clinical and policy relevance

The WHO near-miss tool currently does not consider eclampsia a ‘near-miss’ [13], averting attention from one of the primary causes of preventable maternal and perinatal deaths [1]. With the global increase of maternal deaths due to non-communicable diseases and the evidence of underreporting eclampsia with organ-dysfunction [28,37,38], the WHO may need to reconsider including eclampsia as a separate criterion. The WHO tool provides certain process indicators to address quality-of-care [13]. However, ‘magnesium sulfate coverage’ (i.e., the proportion of women with eclampsia who received MgSO₄) is a poor indicator of the quality-of-care as different LMIC have reported a high prevalence of eclampsia despite the majority of women receiving MgSO₄ [25–27]. Our study complements these findings by demonstrating that MgSO₄ coverage conceals inadequate quality of MgSO₄ provision according to evidence-based recommendations. Specifically, reduction of eclampsia and recurrent fits will not be established if factors such as lower dosage MgSO₄ regimens, no bolus administration in

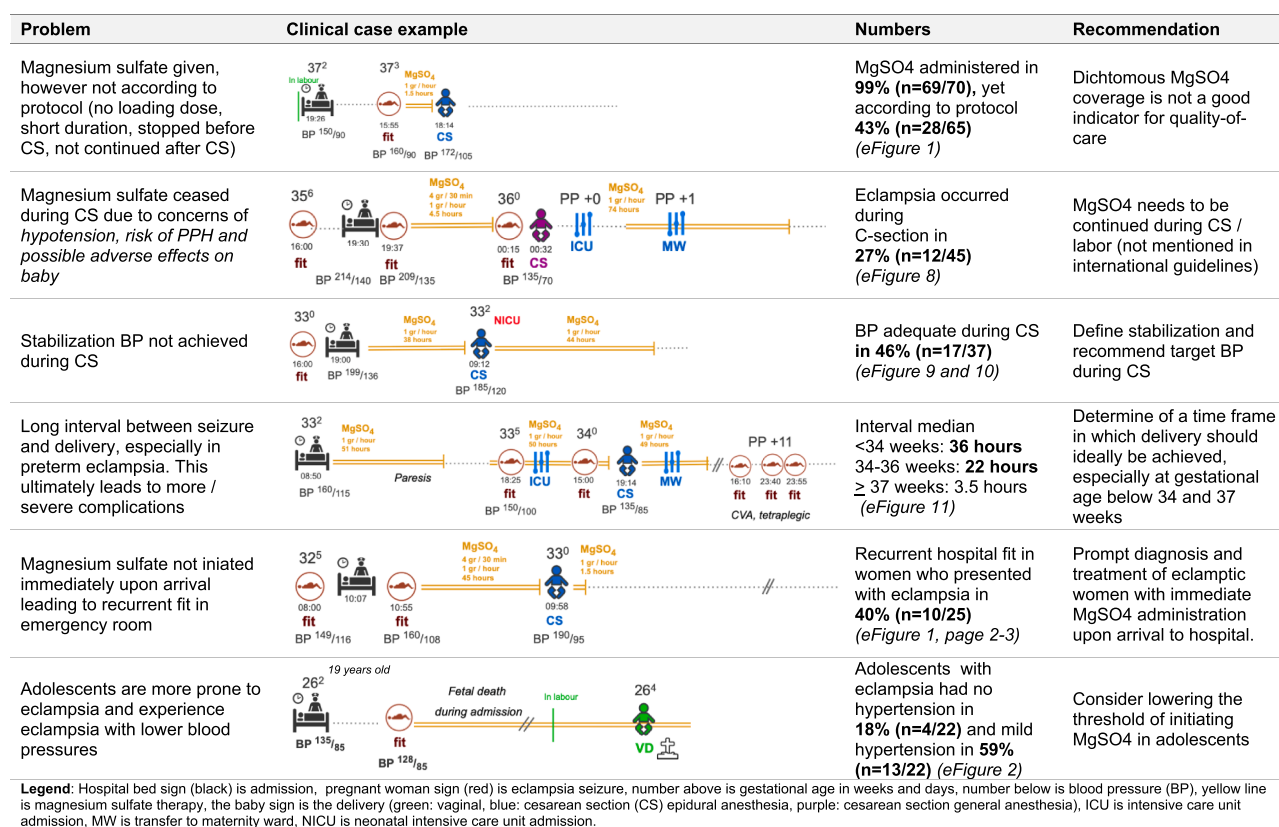


Fig. 1. Summary of problems identified and recommendations of the quality-of-care audits.

recurrent seizures, and the temporary discontinuation of MgSO4 during labor and CS are not revealed. Recent studies in low-income countries have been experimenting with a lower dosage and shorter duration MgSO4 regimens, however, available evidence does not justify introduction in global clinical practice beyond research settings [39–41].

Audits are necessary to reveal shortfalls in prevention and management and develop targeted strategies to improve quality-of-care within countries and between countries. For example, a comparative analysis of two high-income countries (2006) showed that the Netherlands had twice the prevalence (5.4/10,000 deliveries) of eclampsia compared to the United Kingdom (2.7/10,000 deliveries) [42]. Following these results, the Netherlands improved hypertension management and achieved a 70% reduction of eclampsia prevalence (1.8/10,000 deliveries) in ten years [10]. While MgSO4 halves the risk of eclampsia [9], prompt management of severe hypertension is also key in preventing eclampsia and other severe outcomes. In a large three-way randomized controlled trial, three oral antihypertensives were compared in 894 women with severe hypertension [43]. Despite the lack of MgSO4 prevention (12% total, 4% before enrolment), only one woman (0.1%) with severe hypertension developed seizures. Therefore, more emphasis is necessary on the role of timely and tight blood pressure control next to MgSO4 prevention strategies to optimize maternal outcomes [43]. The above-mentioned studies are illustrative examples of the value of international comparison. A vital condition for international comparisons are well-established definitions, and similar core outcome measures [6,44].

4.5. Audit implementation

Implementing continuous audit of maternal mortality and severe morbidity is crucial in improving the quality of maternal health care [10,12,13]. While the maternal mortality committee in Suriname (MaMS) achieved to conduct national maternal death audits continuously since 2015 [45], severe maternal morbidity and perinatal

mortality is audited only periodically, and guidelines are re-evaluated and renewed by the committee every three years. Similar to many other low- and middle-income countries, the lack of financial and human resources is the main challenge in the implementation of continuous audit. The facilitators, which make periodic audits and guideline renewal possible in Suriname, are durable commitment, local ownership and involvement of many local health care providers and national policymakers.

4.6. Recommendations

To eliminate preventable maternal deaths, we need to reduce the prevalence and burden of eclampsia. Suggestions include to (1) develop well-established disease-based criteria and a core outcome set for HDPs, (2) establish international recommendations concerning MgSO4 dosage regimen, blood pressure control, eclampsia stabilization and seizure-to-delivery interval, (3) consider adding eclampsia as a near-miss criterion, and (4) re-evaluate diagnostic criteria for HDPs in adolescents (i.e., the increase of basal blood pressures); Local recommendations to reduce the burden of eclampsia in Suriname include to (1) improve adherence to local evidence-based HDP guidelines, (2) perform facility-based eclampsia audits to improve quality-of-care, (3) establish a national perinatal data registry to monitor trends and disaggregate data, and (4) target inequity by ensuring universal access to quality care and preventing adolescent pregnancies by providing free contraception and safe abortion services.

5. Conclusion

The prevalence of eclampsia and recurrent seizures in Suriname is high. Eclampsia is most common in nulliparous, African-descent adolescents. Adolescents with eclampsia had lower blood pressures than adults, and the increase in basal blood pressure needs to be considered to

prevent diagnostic delay. The 'MgSO₄ coverage' was high (99%) and could not explain the high prevalence of eclampsia and the rate of recurrent seizures. Solely 'MgSO₄ coverage' is not a reliable quality-of-care indicator, as it conceals more important indicators of quality of care, such as MgSO₄ dosage, duration and continuation, stabilization before Cesarean section and seizure-to-delivery interval. These quality-of-care indicators need more international attention in order to reduce the prevalence of eclampsia and recurrent seizures.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

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