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sFlt-1/PlGF and BUN/Albumin Ratios as Novel Prognostic Scores in Critically Ill Preeclampsia Patients in the ICU

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ABSTRACT

Preeclampsia remains a major cause of maternal morbidity and mortality, especially when complicated with multi-organ dysfunction such as renal and pulmonary failure. This study analyzes the utility of the sFlt-1/PlGF and BUN/Albumin ratios as novel prognostic scores for critically ill preeclampsia patients in the ICU. A retrospective observational study of 47 preeclampsia cases was conducted, analyzing the association between these biomarkers and critical clinical outcomes (pulmonary edema, acute kidney injury, mortality, ICU length of stay). Both the sFlt-1/PlGF and BUN/Albumin ratios demonstrated high accuracy as predictors of organ dysfunction, with specific cutoffs and AUC values exceeding 0.7. Implementation of these ratios provides a simple laboratory-based approach for early identification of severe preeclampsia complications in the ICU

KEYWORDS: Preeclampsia, sFlt-1/PlGF Ratio, BUN/Albumin Ratio, Prognostic Score, Maternal Mortality, Acute Kidney Injury, Pulmonary Edema, Biomarker.

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INTRODUCTION

Preeclampsia is a major obstetric complication contributing to maternal and neonatal morbidity and mortality worldwide. International epidemiology reports an incidence of 2–8% of pregnancies, accounting for >46,000 maternal deaths and >500,000 perinatal deaths annually 1] [2]. The risk of severe complications is even higher in developing countries, including Indonesia, where preeclampsia and eclampsia constitute a top cause of maternal death [3].

According to the 2018 National Health Survey of the Ministry of Health of the Republic of Indonesia, the national prevalence of preeclampsia is 2.7% of all pregnancies, with approximately 128,000 new cases annually. The Indonesian Health Profile also shows an upward trend in maternal mortality (MMR) over three years: MMR of 4,221 in 2019 (with hypertensive disorders of pregnancy accounting for 1,066 cases), rising to 4,627 in 2020 (1,110 hypertensive cases), and reaching 7,389 cases in 2021, where hypertension-related complications, especially preeclampsia, are the second most common cause after obstetric hemorrhage [4]. Another report estimates preeclampsia/eclampsia as the cause of 20–24% of maternal deaths in Indonesia, ranking it just after obstetric hemorrhage as the leading cause [5].

Severe complications such as pulmonary edema and acute kidney injury are increasingly observed in severe preeclampsia managed in the ICU [6]. Multinational studies highlight the need for risk assessment models based on simple laboratory biomarkers, allowing for earlier diagnosis and management of organ complications [7]. International validation demonstrates that the sFlt-1/PlGF ratio is a key prognostic biomarker for onset, degree, and organ prognosis in preeclampsia, while the BUN/Albumin ratio is emerging as a predictor of acute outcomes in ICU patients, including those with high-risk pregnancies [8]. This study investigates the combined power of sFlt-1/PlGF and BUN/Albumin ratios as an integrated prognostic scoring model for ICU preeclampsia, aiming to support evidence-based strategies for early detection of organ risk, and thus reduce maternal morbidity and mortality.

METHODS

2.1 Study Design

This was a retrospective observational, cross-sectional analytic study of severe preeclampsia and eclampsia patients admitted to the Intensive Care Unit (ICU) of a national referral hospital in Indonesia from January 2024 to July 2025. The primary aim was to assess the association of the sFlt-1/PlGF and BUN/Albumin ratios with critical organ outcomes, including pulmonary and renal complications as well as maternal mortality.

2.2 Patients and Eligibility

Study subjects were pregnant women diagnosed with severe preeclampsia or eclampsia. Inclusion criteria were: Age ≥18 years,

clinical diagnosis of severe preeclampsia or eclampsia (according to ISSHP 2018 criteria), singleton pregnancy at >28 weeks' gestation, availability of laboratory analysis for sFlt-1, PlGF, BUN, and albumin upon ICU admission, complete outcome data. Exclusion criteria: History of chronic kidney disease, chronic heart failure, severe autoimmune disease, or other major systemic illness prior to pregnancy, severe non-obstetric comorbidities influencing the main parameters incomplete key medical records.

2.3 Sampling

All patients meeting the inclusion criteria during the study period were enrolled consecutively. The minimum sample analyzed was 45 patients, all of whom were pregnant women with severe preeclampsia or eclampsia receiving ICU care.

2.4 Study Variables and Measurement

Independent variables

- sFlt-1/PlGF ratio: Absolute value measured upon ICU admission, assessed by immunoassay (ELISA).
- BUN/Albumin ratio: Calculated from routine blood laboratory analysis on ICU admission.

Dependent variables

- Primary outcomes: Complications of pulmonary edema (diagnosed clinically, by radiology, and P/F ratio), acute kidney injury (KDIGO criteria), maternal mortality, and ICU length of stay (days).
- Additional: Age, BMI, gestational age, initial blood pressure, hemoglobin, platelets, SGOT, SGPT, creatinine, and APGAR scores.

Blood sampling was performed before major interventions; biomarker testing was undertaken in the hospital laboratory. Organ complication diagnoses were verified by the obstetric ICU team using daily medical records.

2.5 Statistical Analysis

All analyses were performed in SPSS v27. Normality was assessed using the Shapiro-Wilk test. Normally distributed data are presented as mean ± SD and evaluated with unpaired t-tests. Non-normally distributed data are presented as median (min–max) and analyzed by Mann-Whitney U-test. Pearson or Spearman correlation was used depending on data distribution. Cut-offs for sFlt-1/PlGF and BUN/Albumin were determined using ROC curves, with sensitivity and specificity calculated accordingly. Statistical significance was set at $p<0.05$.

RESULTS AND DISCUSSION

3.1 Results

3.1.1 Subject Characteristics

A total of 45 patients with severe preeclampsia and eclampsia were admitted to the ICU during the study period. The mean age was 31.87 ± 5.33 years, with most falling within the reproductive age group. The median BMI was 31.63 kg/m² (range: 19.36–52.88), reflecting an obesity trend consistent with established risk factors in organ-complicated preeclampsia. Median gestational age was 34 weeks. Mean systolic BP was 159.8 ± 18.7 mmHg, diastolic 97.7 ± 11.2 mmHg, MAP 117.8 ± 12.5 mmHg. Severe preeclampsia accounted for 68.9% of cases, while eclampsia was found in 11.1%. Mechanical ventilation was required in 31.1% of patients. Median ICU length of stay was 1 day (range: 1–10), but was prolonged in those with complications. Maternal mortality was 6.7%. Neonatal APGAR scores at 1 minute (median 7, range 4–8), and at 5 minutes (median 8, range 5–9), were generally stable, suggestive of successful obstetric resuscitation

Table 1. Baseline Characteristics of ICU Preeclampsia Patients (n=45)

Characteristics	Mean ± SD* / Median (min-max)**	Pulmonary Edema	Non Pulmonary Edema	p value***	Acute Kidney Injury	Non Acute Kidney Injury	p value***
		n = 7 (15.56%)	n = 38 (84.44%)		n = 8 (17.78%)	n = 37 (82.22%)	
Age (years)	31.87 ± 5.33	30.25 ± 5.39	32.22 ± 5.33	0,350	32.13 ± 5.64	31.81 ± 5.34	0,882
Weight (kg)	80.12 ± 17.78	73.13 ± 7.34	81.64 ± 19.05	0,224	74.50 ± 11.44	81.34 ± 18.78	0,330
Height (cm)	155.78 ± 5.96	154.75 ± 8.10	156.00 ± 5.51	0,597	158.75 ± 5.65	155.14 ± 5.90	0,121
Body Mass Index (kg/m2)	31.63 (19.36 - 52.88)	31.15 (26.89 - 34.19)	33.33 (19.36 - 52.88)	0,279	29.88 (21.26 - 38.37)	33.33 (19.36 - 52.88)	0,154
Gestitational ages (weeks)	34 (34 - 42)	34 (34 - 42)	34 (34 - 39)	0,973	34 (34 - 42)	34 (34 - 39)	0,920
Blood pressure (mmHg)							
Systole	159.80 ± 18.70	155.25 ± 16.38	160.78 ± 19.23	0,454	158.13 ± 17.54	160.16 ± 19.16	0,784
Diastole	97.67 ± 11.22	95.88 ± 7.30	98.05 ± 11.94	0,624	96.00 ± 6.33	98.03 ± 12.06	0,648
Mean Arterial Pressure	117.78 ± 12.48	115.25 ± 9.02	118.32 ± 13.15	0,534	116.25 ± 8.91	118.11 ± 13.20	0,707
sFlt-1 (pg/mL)	3100 (1858 - 55068)	4146.50 (3004 - 55068)	3031 (1858 - 19488)	0,016	3229 (2014 - 55068)	3100 (1858 - 19488)	0,678
PlGF (pg/mL)	18.30 (10.60 - 225.00)	21.90 (10.60 - 225.00)	18.20 (11.80 - 82.00)	0,635	17.20 (10.60 - 225.00)	19.10 (11.80 - 82.00)	0,458
sFlt-1/PlGF Ratio	170.47 ± 50.33	218.05 ± 45.61	160.19 ± 45.61	0,002	203.46 ± 52.90	163.34 ± 47.52	0,039
Haemoglobin (g/dL)	11.59 ± 2.02	12.04 ± 1.85	11.49 ± 2.06	0,495	10.01 ± 2.90	11.93 ± 1.64	0,013
Platelate (10^3/µL)	241.40 ± 102.65	247.38 ± 177.72	240.11 ± 82.02	0,858	228.50 ± 122.32	244.19 ± 99.62	0,700
SGOT (U/L)	25 (11 - 874)	61.50 (15 - 874)	23 (11 - 165)	0,090	78 (13 - 874)	23 (11 - 338)	0,102
SGPT (U/L)	15 (5 - 264)	18.50 (5 - 264)	14 (5 - 100)	0,552	28.50 (5 - 264)	14 (6 - 192)	0,389
BUN (mg/dL)	10 (1 - 119)	14 (7.00 - 68.30)	8 (1 - 119)	0,059	27 (13 - 119)	7 (1 - 48)	0,000
Kreatinin (mg/dL)	0.70 (0.30 - 6.80)	1.3 (0.40 - 3.30)	0.70 (0.30 - 6.80)	0,033	2.25 (1.6 - 6.8)	0.60 (0.3 - 1.3)	0,000
Albumin (g/dL)	3.03 (1.70 - 3.56)	2.67 (2.32 - 3.29)	3.07 (1.70 - 3.56)	0,023	2.71 (1.70 - 3.31)	3.07 (2.36 - 3.56)	0,031
BUN/Albumin Ratio	3.24 (0.30 - 70.00)	4.90 (1.22 - 28.82)	2.58 (0.30 - 70.00)	0,050	9.59 (4.15 - 70.00)	2.37 (0.30 - 17.78)	0,000
PF Ratio	255.58 ± 114.23	169.38 ± 97.03	274.22 ± 110.05	0,017	237.75 ± 138.41	259.22 ± 110.17	0,632
Diagnose of Preeclampsia							
Preeclampsia w/o severe features, n(%)	9 (20%)	0 (0%)	9 (20%)		0 (0%)	9 (20%)	
Preeclampsia w/ severe features, n(%)	31 (68.89%)	5 (11.11%)	26 (57.78%)		7 (15.56%)	24 (53.33%)	
Eclampsia, n(%)	5 (11.11%)	2 (4.44%)	3 (6.67%)		1 (2.22%)	4 (8.89%)	
Mechanical Ventilation, n(%)	14 (31.11%)	5 (11.11%)	9 (20%)		4 (8.89%)	10 (22.22%)	
Length of stay in ICU (days)	1 (1 - 10)	2 (1 - 5)	1 (1 - 10)	0,005	2 (1 - 5)	1 (1 - 10)	0,112
Maternal Mortality, n(%)	3 (6.67%)	2 (4.44%)	1 (2.22%)		2 (4.44%)	1 (2.22%)	
Neonates Outcome							
APGAR Score							
1st minutes	7 (4 - 8)	7 (5 - 8)	7 (4 - 8)	0,525	7 (4 - 8)	7 (4 - 8)	0,204
5th minutes	8 (5 - 9)	8 (6 - 9)	8 (5 - 9)	0,301	8 (5 - 9)	8 (5 - 9)	0,215

the Kolmogorov–Smirnov test for normality
* Normally distributed homogeneous data presented with mean ± standard deviation (SD)
** Not Normally distributed homogeneous data presented with median (min - max)
*** Normally distributed homogeneous data using independent sampel T test; Not Normally distributed homogeneous data using Mann-Whitney Test

3.2. Results Grouped by Outcome

3.2.1 Pulmonary Edema

Patients who developed pulmonary edema had significantly higher median sFlt-1/PlGF ratios 218.05 vs 160.19; p = 0.002 and higher BUN/Albumin ratios 4.90 vs 2.58; p = 0.050 compared to those without pulmonary edema. The median PF ratio was also notably lower in the edema group 169.38 vs 274.22; p = 0.017, indicating greater oxygenation impairment.

3.2.2 Acute Kidney Injury (AKI)

AKI occurred in 17.8% of cases. These patients displayed a median sFlt-1/PlGF ratio of 203.46 versus 163.34 in those without AKI (p = 0.039), and a median BUN/Albumin ratio of 9.59 compared to 2.37 (p < 0.001). There was no significant difference in PF ratio between AKI and non-AKI groups.

3.2.3 Maternal Mortality

The sFlt-1/PlGF ratio was highest among cases resulting in maternal death 218.05, with a median BUN/Albumin ratio of 9.59 and a notably low albumin value 2.71 g/dL. The PF ratio was 169.38 in the maternal mortality group, suggesting a marked association of high biomarker levels with fatal outcomes.

3.2.4 Length of ICU Stay

Median ICU length of stay for the entire cohort was 1 day, but extended to 2 days (range 1–5 days; p = 0.005) for patients with complications (either AKI or pulmonary edema), compared to those without complications.

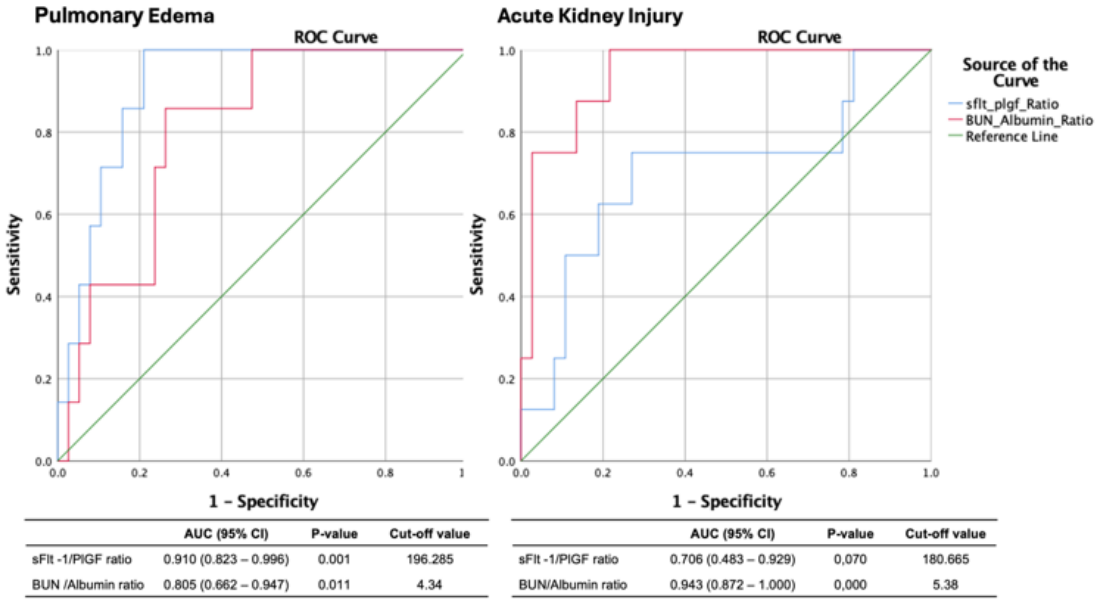
Table 2. Correlation Analysis

		PF ratio	BUN/Albumin Ratio	Acute Kidney Injury	Pulmonary Edema	Severity of PE	Mortality	Length of stay in ICU
sFlt-1/PlGF Ratio	Correlation Coefficient	-0.531***	0.264*	-0.273*	-0.515**	0,040	-0,117	0.306*
	Sig. (1-tailed)	0,000	0,040	0,035	0,000	0,398	0,223	0,020
PF ratio	Correlation Coefficient		-0.376**	0,085	0.401**	0.315*	-0,034	-0.311*
	Sig. (1-tailed)		0,005	0,289	0,003	0,018	0,412	0,019
BUN/Albumin Ratio	Correlation Coefficient			-0.586**	-0.382**	-0.358**	-0.281*	0.380**
	Sig. (1-tailed)			0,000	0,005	0,008	0,031	0,005
Acute Kidney Injury	Correlation Coefficient				0.442**	-0,006	0.342*	-0,240
	Sig. (1-tailed)				0,001	0,484	0,011	0,056
Pulmonary Edema	Correlation Coefficient					0,244	0.377**	-0.495**
	Sig. (1-tailed)					0,053	0,005	0,000
Severity of PE	Correlation Coefficient						0,152	-0.429**
	Sig. (1-tailed)						0,159	0,002

** Correlation is significant at the 0.01 level (1-tailed).

* Correlation is significant at the 0.05 level (1-tailed).

Figure 1. ROC curves for pulmonary edema and AKI



	AUC (95% CI)	P-value	Cut-off value
sFlt -1/PlGF ratio	0.910 (0.823 – 0.996)	0.001	196.285
BUN /Albumin ratio	0.805 (0.662 – 0.947)	0.011	4.34

	AUC (95% CI)	P-value	Cut-off value
sFlt -1/PlGF ratio	0.706 (0.483 – 0.929)	0,070	180.665
BUN/Albumin ratio	0.943 (0.872 – 1.000)	0,000	5.38

Table 3. Diagnostic Accuracy for pulmonary edema and AKI

	Value (95% CI)	
sFlt-1/PlGF Ratio	**Pulmonary Edema**	**Acute Kidney Injury**
Sensitivity	85.71% (42.13% - 99.64%)	75.00% (34.91% - 96.81%)
Specificity	84.21% (68.75% - 93.98%)	72.97% (55.88% - 86.21%)
Positive Likelihood Ratio	5.43 (2.45 - 12.01)	2.77 (1.43 - 5.39)
Negative Likelihood Ratio	0.17 (0.03 - 1.05)	0.34 (0.10 - 1.16)
Positive Predictive Value (PPV)*	50% (31.13% - 68.87%)	37.50% (23.61% - 53.81%)
Negative Predictive Value (NPV)*	96.97% (83.83% - 99.50%)	93.10% (80.00% - 97.85%)
Accuracy*	84.44% (70.54% - 93.51%)	73.33% (58.06% - 85.40%)
BUN/Albumin Ratio		
Sensitivity	71.43% (29.04% - 96.33%)	87.50% (47.35% - 99.68%)
Specificity	73.68% (56.90% - 86.60%)	86.49% (71.23% - 95.46%)
Positive Likelihood Ratio	2.71 (1.34 - 5.51)	6.48 (2.75 - 15.24)
Negative Likelihood Ratio	0.39 (0.12 - 1.27)	0.14 (0.02 - 0.91)
Positive Predictive Value (PPV)*	33.33% (19.75% - 50.39%)	58.33% (37.29% - 76.72%)
Negative Predictive Value (NPV)*	93.33% (81.04% - 97.87%)	96.97% (83.59% - 99.51%)
Accuracy*	73.33% (58.06% - 85.40%)	86.67% (73.21% - 94.95%)

* These values are dependent on disease prevalence.

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Accuracy*	73.33% (58.06% - 85.40%)	86.67% (73.21% - 94.95%)

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DISCUSSION

This study underscores the clinical significance of the sFlt-1/PlGF and BUN/Albumin (BAR) ratios for prognostication in critically ill preeclampsia patients. Notably, a median sFlt-1/PlGF ratio of 218.1 and a median BAR of 4.90 were associated with pulmonary edema, compared to 160.2 and 2.58 in those without pulmonary complications ($p = 0.002$ and 0.050, respectively). Similarly, patients developing AKI displayed markedly higher ratios—sFlt-1/PlGF median 203.5, BAR median 9.59—than peers without AKI (163.3, 2.37; $p = 0.039$ and <0.001). These findings corroborate recent international evidence that high sFlt-1/PlGF and BAR are independently predictive of major organ dysfunction, ICU resource use, and mortality in preeclampsia and other critical illnesses[7][9][10].

Albumin influences BUN primarily through their inclusion in the BAR, which functions as a comprehensive surrogate for renal filtration, nutritional health, and systemic inflammation. In our study, hypoalbuminemia (median albumin 2.71 g/dL in maternal death) co-occurred with high BUN in those with worse outcomes, reflecting a combined burden of catabolism and impaired glomerular filtration. While BUN reflects real-time proteolysis and kidney function, low albumin—seen here in the worst

survivors—frequently signals underlying malnutrition, ongoing inflammation, or diminished hepatic synthesis [11].

At a mechanistic level, hypoalbuminemia reduces oncotic pressure, facilitating vascular fluid extravasation and promoting pulmonary edema, even in the absence of overt overload. This pathophysiology is substantiated by our observed decline in PF ratio among those with both high BAR and low albumin (169.4 vs. 274.2, p = 0.017), highlighting the interplay between nutritional-vascular status and oxygenation failure in preeclampsia. International studies mirror these outcomes, reporting that BAR values above 5, especially in combination with low albumin, are powerful predictors of multi-organ dysfunction and mortality in ICU cohorts [12].

Beyond direct kidney injury, the BAR also encapsulates nutritional and endothelial status, as albumin in critical illness is a negative acute-phase reactant, suppressed by chronic inflammation and protein malnutrition. The high prevalence of both inflammation and malnutrition in our critically ill population (reflected by >33% requiring mechanical ventilation and the ICU median stay rising to 2 days in the complication group) supports the BAR's integrated pathophysiological and prognostic role [12].

In this cohort, the high negative predictive value (NPV) of both sFlt-1/PlGF and BAR (NPV 96.97% for edema, 93.10% for AKI) suggests that values below specific cut-offs can confidently rule out severe complications, ensuring efficient triage and prioritization of interventions. Integrating the BAR with sFlt-1/PlGF offers a multidimensional, evidence-based assessment that reflects renal function, endothelial integrity, nutrition, and inflammation—all major contributors to the morbidity spectrum of preeclampsia [7][9][11].

Thus, our findings reinforce the call for wider adoption of these ratios in ICU preeclampsia protocols, not only as early risk indicators but also as tools for ongoing monitoring and therapy adjustment. In sum, the dataset from this study confirms that a high BAR, when combined with a high sFlt-1/PlGF, identifies patients at greatest risk for pulmonary and renal complications, longer ICU stays, and higher mortality, consistent with and extending the international evidence base to the Southeast Asian context.

CONCLUSION

The sFlt-1/PlGF and BUN/Albumin (BAR) ratios are highly effective, pragmatic tools for the early stratification of pulmonary and renal risks in critically ill preeclampsia patients. In this cohort, a median sFlt-1/PlGF above 180 and a BAR above 4.9 on ICU admission identified patients at significantly elevated risk for pulmonary edema, acute kidney injury, and poorer oxygenation. These associations reflect the interplay of severe angiogenic imbalance, renal dysfunction, chronic inflammation, and compromised nutritional status that underpin multi-organ complications in preeclampsia.

The BAR, in particular, incorporates both renal filtration capacity and systemic status, with high values driven by simultaneous BUN elevation and hypoalbuminemia—a marker of malnutrition, inflammation, and inadequate oncotic pressure—contributing to both pulmonary and renal dysfunction. These findings support the use of BAR, in conjunction with sFlt-1/PlGF, as a routine bedside risk assessment in obstetric ICUs, offering an evidence-based approach to anticipate, triage, and individually tailor the management of organ-threatening complications.

Wider implementation of these ratios in daily critical care practice, especially in resource-limited settings, will allow targeted prevention and management of adverse outcomes, improving overall maternal prognosis in severe preeclampsia and eclampsia.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest relevant to this research.

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