

A prospective study of risk factors of mortality in patients with eclampsia: a single center study

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Abstract:

Objectives: To determine the risk factors affecting the mortality rate in women with eclampsia. **Methods:** This prospective observational cohort included 200 patients who presented with seizures or coma (eclampsia) which could not be attributed to other causes and admitted in the emergency (labour room). The clinical, obstetric examination, and examination pertinent to the signs and symptoms of hypertension and low haemoglobin were done. Laboratory investigations were performed. The fetomaternal outcomes were determined in terms of mortality, mode of delivery, and birth weight. Association of risk of mortality was evaluated in terms of demographic characteristics, obstetric history, delivery details, and signs, symptoms and investigations. P-value <0.05 was considered statistically significant. **Results:** Maternal death occurred in 37 (18.50%) patients. In 29.73% of patients, cause of maternal death was acute pulmonary edema followed by DIC (13.51%). Socioeconomically, low class status, illiteracy, and rural residence carried significantly higher odds of mortality with odds ratio of 1.27, 14.729, and 3.218, respectively. Compared to survivors, those who died had significantly more undelivered pregnancies (40.54% vs. 0%, P<.0001); significantly more instrumental delivery (13.64% vs. 2.45%), and significantly more preterms (54.55% vs. 33.13%). **Conclusion:** In developing countries, eclampsia holds a significant association with maternal deaths, institutional deliveries, and preterm birth. Appropriate caution and management should be done for eclamptic patients to decrease the mortality and improve the fetomaternal outcomes.

Keywords: Eclampsia, fetomaternal, seizures, outcomes, mortality.

Eclampsia remains a worldwide public health problem predominantly in the developing countries¹. WHO reports that there has been a rise in mortality in association with eclampsia with 12% maternal deaths². The associated mortality has been linked with pregnancy related complications in terms of liver failure, kidney failure, neurological damage, and coagulation abnormalities²⁻⁴.

India, being a developing country, with a higher prevalence of eclampsia (3.7%) and a reason for maternal mortality (2.2-23%)², it becomes important to determine the risk factors that increase the maternal mortality in patients with eclampsia so that appropriate measures can be taken, and prognosis can be improved.

Thus, the present study was conducted in a tertiary care institute to determine the risk factors that may increase the mortality rate in women with eclampsia.

Methods

A prospective observational cohort study was conducted in the Department of Obstetrics and Gynaecology in Rajendra Institute of Medical Sciences, Ranchi, from April 2019 to September 2020 where all patients admitted in the emergency labour room with the history of convulsions (eclampsia) were included.

Any patient with chronic hypertension, chronic renal disease, connective tissue disorder, and preeclampsia was excluded.

The study sample size was based on a previous study by Rabiou KA⁵ who observed 19.4% mortality due to eclampsia. Choosing these as reference values with 5.5% margin of error and 5% level of significance the minimum sample size that was required for the study was 199 patients. However, to decrease the margin of error, we enrolled 200 patients.

A duly written and signed informed consent was obtained from all the enrolled patients or their attendants before beginning the study. A detailed history of all the patients were taken which comprised of "age, religion, social economic status, past history, family history, education, residence, gravida and gestational age".

The clinical examination included assessment of "general condition of the patient, vitals -pulse, blood pressure, pallor, icterus, edema and individual organ systems". Obstetric examination: "Symphysiofundal height, abdominal girth, lie, presentation, liquor volume, fetal movement, fetal heart rate" was recorded. Examination was pertinent to note the signs and symptoms of hypertension and low haemoglobin such as pallor and edema. Blood pressure was recorded (systolic-SBP and diastolic-DBP) for all women.

The patients were subjected to blood investigations:

- a. Complete blood count
- b. Platelet count, bleeding time(BT) and clotting time (CT)
- c. Urea, creatinine
- d. Uric acid
- e. Urinary total protein
- f. Total bilirubin
- g. Liver enzymes - aspartate amino transferase (AST/SGOT) and alanine amino transferase (ALT/SGPT).
- h. Lactate dehydrogenase (LDH).
- i. Blood grouping
- j. Serum electrolyte
- k. Sonographic evaluation of fetoplacental profile.

The patients were followed up for the outcomes of pregnancy in terms of "induction of labour, term/pre-term, type of delivery, indication of caesarean delivery and mortality". The induction of labour was done as per the hospital protocol by Cerviprime gel or Misoprost. The Bishop score was also recorded at the time of labor and delivery. The assessment and diagnosis of Eclampsia was made according to the criteria of ACOG Guidelines.²

The eclampsia in patients were managed as per the hospital protocol by using magnesium sulphate, as per the Pritchard regimen(IM)- 4gm (20% solution) IV over 3-5 minute followed by 10 gm (50% solution), deep IM (5 g in each buttock) followed by maintenance dose 5gm (50% solution) IM 4 hourly in alternate buttock.²

The neonatal outcomes were followed in terms of baby weight. The outcome measures were maternal mortality rate and the risk factor associated with it.

Statistical analysis: The data presentation was done in the tables and graphs after entering into "Microsoft EXCEL spreadsheet". Kolmogorov-Smirnov test was used to assess data normality wherein the non-normalized data was analyzed using "non-parametric tests". The association of the age, hemoglobin, blood pressure, BT, CT, blood urea, serum creatinine, SGOT, SGPT, SAP, serum LDH, serum uric acid, platelets count was done using "Mann-Whitney Test". The association of religion, term/preterm, serum electrolytes was done using "Chi-Square test". Fisher's exact test was used for analysis of socio-economic status, education, area of residence, antenatal status, past history of

hypertension, obstetric history, undelivered, mode of delivery, indication of LSCS, general condition, proteinuria, fetal outcome. Odds ratio was calculated for determining significant predictors of maternal death.

The final analysis was done by “Statistical Package for Social Sciences (SPSS) software, IBM manufacturer, Chicago, USA, version 21.0”. For statistical significance, “p value of less than 0.05” was considered statistically significant.

Results

Mean age of the patients in the study was 22.72 ± 4.2 years with no significant difference in the age of patients who died and survived ($p=0.749$). Most of the patients were Hindus (65.50%), belonged to low socioeconomic status (80.00%), and were from rural area (73.50%). Socioeconomically, low class status, illiteracy and rural residence carried a significantly higher odds of mortality with odds ratio of 1.27, 14.729, and 3.218, respectively (table 1).

Table 1: Association of socio-demographic characteristics with mortality					
Socio-demographic characteristics	Survivors (n=163)	Died (n=37)	Total	P value	Odds ratio (95% CI)
Age(years)	22(20-25)	22(20-23)	22(20-24)	0.749*	0.999(0.917 to 1.087)
Religion					
Hindu	107 (65.64%)	24 (64.86%)	131 (65.50%)	0.551 [‡]	1
Christian	35 (21.47%)	6 (16.22%)	41 (20.50%)		0.803(0.309 to 2.086)
Muslim	21 (12.88%)	7 (18.92%)	28 (14%)		1.531(0.59 to 3.972)
Socio-economic status					
Upper	6 (3.68%)	1 (2.70%)	7 (3.50%)	0.002 [†]	1
Low	124 (76.07%)	36 (97.30%)	160 (80%)		1.27(0.184 to 8.785)
Middle	33 (20.25%)	0 (0%)	33 (16.50%)		0.065(0.002 to 1.96)
Education					
Literate	83 (50.92%)	2 (5.41%)	85 (42.50%)	<.0001 [†]	1
Illiterate	80 (49.08%)	35 (94.59%)	115 (57.50%)		14.729(3.911 to 55.474)
Area of residence					
Urban	49 (30.06%)	4 (10.81%)	53 (26.50%)	0.022 [†]	1
Rural	114 (69.94%)	33 (89.19%)	147 (73.50%)		3.218(1.129 to 9.177)
Antenatal status					
Unbooked	113 (69.33%)	36 (97.30%)	149 (74.50%)	0.0001 [†]	1
Booked	50 (30.67%)	1 (2.70%)	51 (25.50%)		10.827(2.014 to 58.202)
Past history of hypertension					
No	150 (92.02%)	33 (89.19%)	183 (91.50%)	0.526 [†]	1
Yes	13 (7.98%)	4 (10.81%)	17 (8.50%)		1.498(0.469 to 4.778)
* Mann Whitney test, † Fisher's exact test, ‡ Chi square test					

* Mann Whitney test, [†] Fisher's exact test, [‡] Chi square test

Table 2: Association of obstetric history with mortality					
Obstetric history	Survivors (n=163)	Died (n=37)	Total	P value	Odds ratio (95% CI)
Parity					
Primipara	9 (5.52%)	3 (8.11%)	12 (6%)	0.631 [†]	1
Multipara	5 (3.07%)	1 (2.70%)	6 (3%)		0.74(0.072 to 7.61)
Primigravida	116 (71.17%)	23 (62.16%)	139 (69.50%)		0.548(0.142 to 2.114)
Multigravida	33 (20.25%)	10 (27.03%)	43 (21.50%)		0.851(0.198 to 3.647)
Type of eclampsia					
Antepartum	145 (88.96%)	35 (94.59%)	180 (90%)	0.38 [†]	1
Postpartum	18 (11.04%)	2 (5.41%)	20 (10%)		0.554(0.136 to 2.251)
† Fisher's exact test					

[†] Fisher's exact test

Among the total population, majority were primi gravida (69.5%) with parity showing no significant association with mortality (table 2). Clinically, edema was present in 82.00% patients. Proteinuria showed 2+ in 55.50% patients and 3+ in 25% patients. Pallor was mild and moderate in 39% and 38% patients, respectively (table 2). Blood group of 66.50% of patients was O+ve followed by B+(14.50%), A+(12.50%) and AB+(6%). Only 1 patient had O-ve blood group. Antepartum eclampsia (APE) was present in 90% cases and postpartum eclampsia (PPE) was present in 10% cases. The type of eclampsia showed no significant association with mortality as shown in table 2.

Table 3: Association of delivery details with mortality					
Delivery details	Survivors	Died	Total	P value	Odds ratio (95% CI)
Undelivered/delivered					
Delivered	163 (100%)	22 (59.46%)	185 (92.5%)	<.0001 [†]	1
Undelivered	0 (0%)	15 (40.54%)	15 (7.50%)		225.267(11.886 to 4269.193)
Mode of delivery					
Vaginal delivery	106 (65.0%)	16 (72.73%)	122 (65.9%)	0.018 [‡]	1
Instrumental delivery	4 (2.45%)	3 (13.64%)	7 (3.78%)		5.02(1.033 to 24.409)
LSCS	53 (32.52%)	3 (13.64%)	56 (30.27%)		0.422(0.126 to 1.414)
Indication of LSCS					
APE+FD+Severeoligohydramnion	1 (1.89%)	0 (0%)	1 (1.79%)	0.486 [‡]	1
APE+Failed induction	1 (1.89%)	0 (0%)	1 (1.79%)		1(0.002 to 602.58)
APE+Failedinduction+IUD	0 (0%)	1 (33.33%)	1 (1.79%)		9.002(0.015 to 5425.859)
APE+Fetal distress	3 (5.66%)	0 (0%)	3 (5.36%)		0.429(0.001 to 124.808)
APE+IUGR+Fetal distress	1 (1.89%)	0 (0%)	1 (1.79%)		1(0.002 to 602.58)
APE+Primi breech	1 (1.89%)	0 (0%)	1 (1.79%)		1(0.002 to 602.58)
APE+severeoligohydramnion	1 (1.89%)	0 (0%)	1 (1.79%)		1(0.002 to 602.58)
Cephalopelvic disproportion	2 (3.77%)	0 (0%)	2 (3.57%)		0.6(0.002 to 210.031)
Compound presentation+fetal distress	1 (1.89%)	0 (0%)	1 (1.79%)		0.6(0.002 to 210.031)
CPD+APE	1 (1.89%)	0 (0%)	1 (1.79%)		1(0.002 to 602.58)
CPD+Fetal distress	1 (1.89%)	0 (0%)	1 (1.79%)		1(0.002 to 602.58)
Face presentation+APE	1 (1.89%)	0 (0%)	1 (1.79%)		1(0.002 to 602.58)
Failed induction	4 (7.55%)	0 (0%)	4 (7.14%)		0.333(0.001 to 88.533)
Failed induction+APE	2 (3.77%)	0 (0%)	2 (3.57%)		1(0.002 to 602.58)
Failed induction+Fetal distress	2 (3.77%)	0 (0%)	2 (3.57%)		0.6(0.002 to 210.031)
Fetal distress	22 (41.5%)	1 (33.33%)	23 (41.07%)		0.2(0.002 to 25.067)
Fetal distress+placenta previa	1 (1.89%)	0 (0%)	1 (1.79%)		1(0.002 to 602.58)
Hand prolapse	1 (1.89%)	0 (0%)	1 (1.79%)		1(0.002 to 602.58)
IUGR+Severe oligohyramanion	1 (1.89%)	0 (0%)	1 (1.79%)		1(0.002 to 602.58)
Obstucted labour	2 (3.77%)	1 (33.33%)	3 (5.36%)		1.8(0.011 to 293.543)
Previous CS + ST	2 (3.77%)	0 (0%)	2 (3.57%)		0.6(0.002 to 210.031)
Severe oligohyramnion+fetal distress	1 (1.89%)	0 (0%)	1 (1.79%)		1(0.002 to 602.58)
Twin with 1st breech with fetal distress+oligohydramnion	1 (1.89%)	0 (0%)	1 (1.79%)		1(0.002 to 602.58)
Term/preterm					
Term	109 (66.8%)	10 (45.45%)	119 (64.3%)	0.049 [‡]	1
Preterm	54 (33.1%)	12 (54.55%)	66 (35.68%)		2.392(0.985 to 5.811)
† Fisher's exact test. ‡ Chi square test					

[†] Fisher's exact test, [‡] Chi square test

Table 4: Association of signs, symptoms and investigations with mortality					
Signs, symptoms and investigations	Survivors (n=163)	Died (n=37)	Total	P value	Odds ratio (95% CI)
General condition					
Conscious	71 (43.56%)	4 (10.81%)	75 (37.50%)	0.0001 [†]	1
Unconscious	92 (56.44%)	33 (89.19%)	125 (62.50%)		5.754(2.038 to 16.244)
Edema					
Absent	31 (19.02%)	5 (13.51%)	36 (18%)	0.431 [‡]	1
Present	132 (80.98%)	32 (86.49%)	164 (82%)		1.405(0.519 to 3.802)
Proteinuria					
Trace	1 (0.61%)	0 (0%)	1 (0.50%)	0.722 [†]	1
1+	28 (17.18%)	9 (24.32%)	37 (18.50%)		1(0.01 to 98.209)
2+	91 (55.83%)	20 (54.05%)	111 (55.50%)		0.672(0.007 to 63.722)
3+	42 (25.77%)	8 (21.62%)	50 (25%)		0.6(0.006 to 58.922)
4+	1 (0.61%)	0 (0%)	1 (0.50%)		1(0.002 to 602.577)
Serum electrolyte					
WNL	152 (93.25%)	27 (72.97%)	179 (89.50%)	0.0003 [‡]	1
Deranged	11 (6.75%)	10 (27.03%)	21 (10.50%)		5.063(1.962 to 13.068)
Hemoglobin (gm/dL)	10.2(9.5-10.5)	9.5(8-10.2)	10(9.3-10.5)	0.002 [*]	0.614(0.469 to 0.803)
Systolic blood pressure(mm of Hg)	150(150-160)	140(110-160)	150(140-160)	0.001 [*]	0.967(0.95 to 0.984)
Diastolic blood pressure(mm of Hg)	110(100-110)	80(70-110)	110(90-110)	<.0001 [*]	0.936(0.914 to 0.96)
BT(Bed side in minutes)	2.25(1.5-2.667)	1.5(1.333-2.333)	1.83(1.5-2.667)	0.01 [*]	0.567(0.36 to 0.894)
CT(Bed side in minutes)	4.83(4.667-5.583)	4.67(3.833-5.5)	4.83(4.5-5.5)	0.147 [*]	0.859(0.593 to 1.245)
Blood urea(mg/dL)	45(40-59)	55(48-70)	48(40-60)	0.007 [*]	1.022(1.007 to 1.037)
Serum creatinine(mg/dL)	1(0.7-1.35)	1.2(1-1.5)	1(0.8-1.4)	0.003 [*]	1.585(1.101 to 2.282)
SGOT(U/L)	50(40-67)	57(45-89)	50(42.75-70)	0.014 [*]	1.002(1 to 1.004)
SGPT(U/L)	54(43-70)	56(49-80)	55(43.75-75)	0.081 [*]	1.004(1 to 1.008)
SAP(U/L)	140(120-205)	213(130-320)	146.5(120-223.25)	0.001 [*]	1.003(1.001 to 1.005)
Serum LDH(IU/L)	460(420-530)	500(440-700)	475(428.25-550)	0.044 [*]	1.002(1 to 1.003)
Serum uric acid(mg/dL)	6.1(5.4-6.5)	6.4(6.1-7.1)	6.1(5.575-6.625)	0.001 [*]	1.019(0.964 to 1.076)
Platelets count(lakh/cmm)	1.9(1.4-2.9)	1(0.8-1.2)	1.8(1.2-2.9)	<.0001 [*]	0.167(0.08 to 0.348)
* Mann Whitney test, [†] Fisher's exact test, [‡] Chi square test					

In the present study, induction for labour was done in 53.30% patients for which cerviprime gel and cerviprime gel/misoprost were used in 96.91% and 3.09% patients, respectively. Mean Bishop score of study subjects was 6.09 ± 2.61 . Mean admission-delivery interval (hour) of study subjects was 4.71 ± 2.67 .

Maternal death occurred in 37 (18.50%) patients. In 29.73% of patients, cause of maternal death was acute pulmonary edema followed by disseminated intravascular coagulation (DIC, 13.51%), cerebrovascular accident (CVA, 10.81%), cardiac failure (8.11%), septic shock (8.11%), acute pulmonary edema + severe anaemia (5.41%), acute renal failure (5.41%), and septicemia (5.41%).

Compared to survivors, those who died had significantly more unconscious patients (89.19% vs. 56.44%, $P=0.0001$); significantly more deranged serum electrolyte (27.03% vs. 6.75%, $P=0.0003$); significantly higher blood urea (mg/dL) (55 vs. 45), serum creatinine (1.2 vs. 1, $P=0.003$), SGOT (U/L) (57 vs. 54, $P=0.014$), SAP (U/L) (213 vs. 140, $P=0.001$), serum LDH (IU/L) (500 vs. 460, $P=0.044$), serum uric acid (mg/dL) (6.4 vs. 6.2, $P=0.001$); and significantly lower haemoglobin (gm/dL) (9.5 vs. 10.2, $P=0.002$), platelets count (lakh/cmm) (1 vs. 1.9, $P<0.0001$), SBP (140 vs. 150, $P=0.001$), DBP (80 vs. 110, $P<0.0001$), BT (Bed side in minutes) (1.5 vs. 2.25, $P=0.01$); and comparable edema ($P=0.431$), proteinuria ($P=0.722$), and CT (Bed side in minutes) ($P=0.147$) (table 3).

Compared to survivors, those who died had significantly more instrumental delivery (13.64% vs. 2.45%), and significantly more preterms (54.55% vs. 33.13%, $P=0.049$), and comparable indication of caesarean (CS) (table 4).

Discussion

Severe preeclampsia/eclampsia has major effects on maternal and neonatal health, with 50,000–100,000 deaths worldwide each year, as well as significant foetal and neonatal morbidity and mortality. These pregnancy disorders are more common in low and middle-income countries². Eclampsia is a life-threatening pregnancy complication characterised by tonic-clonic seizures (convulsions), which usually emerge in a woman with pre-eclampsia. Convulsions and coma that occur during pregnancy but are not caused by a pre-existing or organic brain disorder are referred to as eclampsia. The complications related to eclampsia are pulmonary edema, cerebrovascular accidents, disseminated intravascular coagulation, HELLP syndrome, and hepatic and renal failure³.

The proportion of maternal mortality (especially in relation to hypertension in pregnancy) is very high in India⁵. Mortality rate in our study was 18.5%. Higher mortality rate was seen in a study conducted at Eastern India by Das R et al⁶, as eclampsia was responsible for 43.4% of the maternal deaths; the case fatality rate was 4.96%. Sinha et al⁷ reported mortality rate of 25.3% in Eastern India. In another study conducted at North-eastern state of India by Nobis PN et al⁸, mortality rate of eclampsia was 4.1%.

Literature also shows that mortality remain high in other developing countries as seen in other study conducted in countries like Nigeria, Bangladesh and Morocco. In a study conducted at Nigeria by Rabiou et al⁵, out of 143 deaths, eclampsia accounted for 28.7% deaths. Olatunji et al⁹ reported a mortality rate of 20% in western Nigeria, and Kullima et al¹⁰ found mortality rate of 22.3% in northern Nigeria. In a study conducted at Dhaka, mortality rate was 14.70%,¹¹ whereas in a study from Morocco, mortality rate of 6.7% was found¹². In contrast, mortality rate remains low in developed countries with reports from UK (0%)¹³ and Saudi Arabia (0%)¹⁴. The rates of maternal mortality due to eclampsia are very lower in the developed countries possibly due to the well-developed healthcare facilities.

The factors affecting mortality in developing countries remain linked with socioeconomic status of the population. Validating this fact, we found that low class status, illiteracy and rural residence carried significantly higher odds of mortality (OR: 1.27, 14.729, and 3.218, respectively). Majority of the women were Hindus, and from low socioeconomic status and rural area. Similarly, Rabiou et al⁵ found that majority of maternal deaths were more uneducated (53.7% vs. 48.8%), Christians (73.2% vs. 71.8%), and unemployed (48.8% vs. 26.5%) ($P>0.05$). Das R et al⁶ also found that those who died were from lower socioeconomic class, illiterate, and rural areas. Similar findings were reported by Ragasudha et al¹⁵, as all women were from low socioeconomic status and majority from rural area.

Lack of education, superstitious as well as traditional beliefs are the factors that are accountable for delayed transfer of women to healthcare facilities in developing countries. In India, several women with problems in pregnancy present first to traditional “*dais*” and then only go to the hospital as a last choice if complications arise. Another factor responsible for delayed presentation is the financial constraint. Our study shows that derangements in the various baseline investigations of liver and kidney profile may help in determining the risk of mortality. Among other studies, Sak ME et al¹⁶ also found that deranged values of ALT, AST, LDH levels may underline the risk for maternal mortality.

Along with levels of laboratory parameters, systolic hypertension due to eclampsia is also one of the etiologic factors for enhanced mortality risk in mothers as was observed in our study. In concordance, Schutte JM et al¹⁷, showed an association between hypertension and increase in mortality based on intracerebral bleeding. Lower values of hematocrit and haemoglobin were additional etiologic factors for increased rate of mortality.

Moreover, the total platelet counts may also affect the maternal outcomes as was observed in our study. Getaneh et al¹⁸ also found that platelet count <50,000 cells/mm³ and platelet count 50,000-99,000 cells/mm³ were strong predictors of adverse maternal outcomes among mothers with eclampsia. In a study conducted at Zimbabwe by Ngwenya et al¹⁹, the adverse maternal outcomes increased for platelet <50,000 cells/mm³ and 50,000-99,000 cells/mm³. Similar findings were also reported by Rebahi et al²⁰, as an increase in adverse maternal outcomes was found due to decrease in platelet counts. The strong association between adverse outcomes and low platelet count can be explained by the fact that low platelet count result in enhanced risk of bleeding in the brain (including increased intracranial pressure, intracranial hemorrhage, stroke, and brain herniation) as well as other organs.

Because of mortality, even the outcomes of eclamptic population remain adverse. We found that instrumental deliveries and preterm deliveries were significantly increased owing to unconscious nature and increasing complications among the women. In corroboration, Sinha et al⁷ found that there were significantly more cases of preterm deliveries (17.3% vs. 13.8%). This necessitates an early intervention in terms of delivery of the baby for eclamptic women.

Limitations: The findings of the present study cannot be generalized as study site was facility-based, particularly in low-resource settings. Status of maternal smoking was also not considered, which may be a factor for pre-eclampsia/eclampsia. Lastly, the follow-up was short which might play a limitation in comparison to some previous studies.

Conclusion

In low and middle-income countries, eclampsia is significantly associated with maternal death, instrumental deliveries, and preterm birth. The “mortality rate” among our study patients were 18.5%. At the individual level, a number of sociodemographic (such as low class status, illiteracy, and rural residence), obstetric and deranged laboratory parameters were significant risk factors for mortality in eclampsia, with hypertension and severe anemia posing the high risks on mortality. Eclampsia was associated with more undelivered cases, instrumental deliveries, and preterm deliveries. It is advised that effective treatments targeting risk factors be implemented, as well as the provision of high-quality healthcare services and collaborative efforts be made to improve the fetomaternal outcomes.

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