Perinatal Outcome in Pregnanacies Associated with Hypertension: A Prospective Cohort Study in a Rural Tertiary Care Teaching Hospital of North India

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ABSTRACT

Objective: The objective of the study is to know type of hypertension affecting pregnant women and impact on perinatal outcome.

Subject and Methods: This is a prospective cohort study; 120 women with hypertensive disorders of pregnancy (HDP) at gestation ≥28 weeks who delivered in our institute were enrolled. Sociodemography, gestational age, mode of delivery, APGAR, birth weight, fetal growth restriction (FGR), and perinatal outcome were recorded. Mean ± standard deviation or proportions, analysis of variance, Chi-square test, and odds ratio were used for statistical analysis. Results: Preeclampsia (PE) was most prevalent hypertensive disorder of pregnancy (44.2%), followed by eclampsia (27.5%), gestational hypertension (23.3%), and chronic hypertension (CH) (5.0%). In PE group, 61.8% had FGR, 65.5% newborns were preterm, 74.6% had low birth weight, and 54.1% needed neonatal intensive care unit (NICU) admission. In eclampsia group, 42.9% had fetal growth restriction, 65.7% preterm, 80% low birth weight, and 78.6% NICU admission. PE women delivered more fetal growth-restricted babies with odd ratio of 2.37 (95% confidence interval [CI]: 1.15, 4.9) and at lower gestation with odd ratio of 2.00 (95% CI: 0.95, 4.21). Eclampsia group had more newborn with low APGAR 1 min, NICU admissions, and those requiring ventilator with odds ratio of 3.10 (95% CI: 1.37, 7.03), 4.48 (95% CI: 1.64, 12.24), and 4.09 (95% CI: 1.6, 10.46), respectively. Perinatal mortality was 10, 9, and 2 in eclampsia, PE, and gestational hypertension groups, respectively, with overall rate of 16.9%. PE and eclampsia comprised 71.70% of HDP but contributed 90.5% of all perinatal deaths. Conclusion: Preeclampsia-eclampsia is associated with increased risk of adverse perinatal outcomes as compared to gestational and CH, necessitating screening, vigilant antenatal care, timely intervention, and referral.

Keywords: Chronic hypertension, eclampsia, gestational hypertension, hypertensive disorders of pregnancy, perinatal outcome, preeclampsia

INTRODUCTION

Globally, hypertensive disorders of pregnancy (HDP) are one of the major causes of perinatal and maternal morbidity and mortality.1-3 These disorders are characterized by increase in blood pressure (BP) which may be present before or appear for the first time during pregnancy after 20 weeks with or without proteinuria or evidence of multiorgan involvement and have been classified into preeclampsia (PE) and eclampsia syndrome, chronic hypertension (CH), PE superimposed on CH, and gestational hypertension.4 The HDP may complicate 5%-10% of all the pregnancies5 with the prevalence of 6.9%-7.9%6,7 in India. Studies have shown that HDP accounts for around 16% of 2.6 million stillbirths8,9 and 15% of perinatal deaths globally.10,11 Higher rates of adverse perinatal outcome such as preterm delivery, low birth weight, birth asphyxia, stillbirth, and early death have been reported worldwide in women having HDP.12 Prematurity and preterm birth are documented as the most common cause of perinatal death in Indian women with HDP13. The present study was...
conducted with the aim to know the type of hypertension affecting the pregnant women and perinatal outcome in rural low middle-income population of North India.

**Subjects and Methods**

**Study design**
Prospective cohort study.

**Study period**
December 2017 to November 2018.

**Sample size determination**
The sample size estimation was based on the prevalence of HDP in the literature and was calculated by the formula

\[ n = \frac{Z^2 \times (p) \times (1-p)}{c^2} \]

Where \( Z = Z \) value (e.g., 1.96 for 95% confidence level), \( p \) = percentage expressed as decimal, and \( c \) = the confidence interval (CI) expressed as decimal. With estimated the prevalence of HDP among Indian women between 6.9% and 7.9%, the required calculated sample size for our study was 99 to 112 with precision of 5% and CI of 95%. Therefore, a cohort of 120 parturient with HDP during the study period gave an adequate sample.

**Study population**
Pregnant women with associated hypertension and period of gestation (POG) ≥28 weeks who delivered in our institute.

**Main outcome measures**
Type of hypertension affecting the pregnant women and impact on perinatal outcome.

**Methods**
After obtaining written informed consent, this study was conducted at MMIMSR, a rural tertiary care teaching hospital of North India. This hospital has 24 h intensive care unit (ICU), neonatal ICU (NICU), labor room HDU, and blood bank facilities and caters to the local rural population and adjoining rural areas of neighboring state UP. All women who fulfilled the inclusion criteria were identified and followed up till delivery and perinatal outcome noted.

**Data collection**
For each eligible participant data pertaining to sociodemography (age, literacy, place of residence, booked, or referred) were obtained in a structured predesigned proforma by the second author. Detailed obstetrical history including state of gravida, duration of pregnancy, presenting complaint, and previous medical history was noted. All participants underwent general physical and detailed obstetrical examination. Routine blood investigations, urine examination for albumin, and ultrasonography were performed. BP monitoring was done at least 4 h apart or earlier, and parturients were managed as per hospital protocol. All participants were delivered according to the severity of disease/duration of pregnancy and were monitored during labor and postpartum period.

Variables of perinatal outcome included gestational age, fetal growth restriction, live/stillbirth, preterm birth (<37 weeks or <34 weeks), mode of delivery, APGAR at 1 and 5 min of birth by attending pediatrician; gender, birth weight, small for gestational age (SGA), and early neonatal death were recorded. Need of ventilator and NICU admission was decided by the pediatrician. Perinatal outcome was analyzed between their groups of HDP. Variables used to describe perinatal outcome were preterm, SGA, low birth weight, stillbirth, early neonatal death, and perinatal mortality.

Data collected was subjected to descriptive analysis with mean ± standard deviation (SD) or proportions. Analysis of variance was applied to compare the continuous variables. Categorical variables were analyzed using Chi-square test. Odds ratio (OR) and 95% CI were computed to assess the risk. A probability value \( P < 0.05 \) was considered statistically significant.

**Operational definitions**
Perinatal mortality (stillbirth plus neonatal deaths) is defined as deaths among fetuses weighing 1000 g or more at birth (28-week gestation) who die before or during delivery or within 7 days of delivery.\[14\]

This study was approved by the Institutional Ethics Committee and was a part of a trial registered with Central Trial Registry India; CTRI/2018/05/014057.

**Results**
We analyzed the perinatal outcome among 120 women with HDP with rural background who delivered 124 babies (included 4 twins) at or after 28 weeks of gestation during study period. Out of 120 participants, 106 (88.3%) were unbooked. Most of the participants (113/120, 94.12%) belonged to low and low-middle socioeconomic status with the incidence of HDP 8.76%. There were 108 live births, 16 stillbirths, and 5 neonatal deaths within 7 days with overall perinatal mortality of 16.9%. Table 1 shows the details of the women and the newborn.

Table 2 depicts that the most prevalent HDP was PE 53 (44.2%) followed by eclampsia 33 (27.5%), gestational hypertension 28 (23.3%), and CH 6 (5.0%). The mean maternal age was significantly higher in CH group 32.33 ± 5.44 years (\( P = 0.020 \)). The minimum mean POG at birth was 34.21 ± 3.97 weeks in E and the maximum in GH (37.30 ± 2.61) with significant statistical difference (\( P = 0.007 \)). Significantly more number of low birth weight babies was seen in PE and E groups as compared to GH and CH (\( P = 0.001 \)). Low 1 and 5 min APGAR was seen in E and PE which was significant (\( P = 0.014 \) and \( P = 0.026 \)). Best R score was noted in CH group.

Table 3 highlights that the type of hypertension was not significantly affected by the gravidity (\( P = 0.546 \)). POG <37 weeks at the time of delivery was seen significantly more in PE and E groups (\( P = 0.012 \)). Women delivering at POG <34 weeks were 33 (27.5%), 15 in E, 14 in PE, 3 in GH, and 1 in CH.
Table 4 shows that the number of babies born prematurely was 71 (57.3%) out of which 36 (50.7%) delivered at <34 weeks of gestation and were contributed significantly by PE and E groups ($P = 0.0066$). Out of 124 births, 50% ($n = 62$) showed fetal growth restriction (FGR) with group-wise distribution of 61.8% in PE, 42.9% in E, 42.9% in GH, and 16.7% in CH women. APGAR <7 at 1 min was seen significantly more in women with E and PE ($P = 0.0003$). APGAR (4–6) at 1 min improved significantly in PE and eclampsia group babies and became statistically comparable at 5 min ($P = 0.001, P = 0.002$, respectively) but neonates having low APGAR (0–3) at 1 min remained the same at 5 min. Out of total 80 (64.5%) low birth babies, percentage in E, PE, CH, and GH was 80%, 74.6%, 33.3%, and 32.2%, respectively, with statistically significant difference ($P = 0.0014$). Of 108 live newborn, NICU admission was required in 58 (53.7%) and NICU admission was needed in 78.6%, 54.1%, 50%, and 26.9 above groups. Ventilator was required in 27 (25%) of live newborn. E and PE newborns contributed maximally to ventilator and NICU. Out of total 16 stillbirths, 7 each occurred in E and PE groups and 2 in GH group.

Table 5 shows the OR and 95% CIs for Gestational Hypertension, Chronic Hypertension, Preeclampsia and Eclampsia with respect to gravidity, period of gestation, APGAR at 1 minute, low birth weight, neonatal intensive care unit admission, ventilator requirement, and fetal growth restriction. Women with PE with OR 1.12 (95% CI: 0.54, 2.34) and 1.23 (95% CI: 0.52, 2.95), respectively. Women with PE and E are at increased risk of preterm delivery, OR = 2.00 (95% CI: 0.95, 4.21) and 1.49 (95% CI: 0.65, 3.40). Eclamptic women were at highest risk for low 1 min APGAR score, OR = 3.10 (95% CI: 1.37, 7.03). Mothers with E and PE are more likely to have low birth weight babies as compared to CH and GH with OR = 2.84 (95% CI: 1.12, 7.20) and 2.25 (95% CI: 1.04, 4.87). Newborn of eclamptic mothers were significantly higher risk for NICU admission and ventilator requirement (OR = 4.48 [95% CI: 1.64, 12.24] and 4.09 [95% CI: 1.6, 10.46], respectively). Preeclamptic mothers were at significantly higher risk for FGR (OR = 2.37 [95% CI: 1.15, 4.9]).

**DISCUSSION**

In India, the perinatal mortality rate is 26/1000 births.[15] It ranges from 16/1000 births in urban areas to 28/1000 births in rural areas.[16] Different studies done in India show HDP as a leading cause of adverse perinatal outcome and mortality.[17-19]

In our study, the perinatal mortality rate was 16.9% because of HDP which is similar as reported by other authors from 12.4% to 20.4%.[3-17,21] Types of HDP seen in our study are similar to the findings of Sharma et al. who observed 6.92% HDP with PE contributing to 50.2%, E – 35.7%, GH – 12.5%, and CH – 1.6%.[17]

We observed perinatal mortality of 28.6% in women with eclampsia followed by 16.4% in PE and 7.1% in gestational hypertension suggesting that women in eclampsia and PE were at highest risk for an adverse perinatal outcome which is in accordance with the observations of Panda et al.[19]

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**Table 1: Maternal (n=120) and Neonatal (n=124) details**

| Variable          | Maternal | Minimum | Maximum | Mean ± SD |
|-------------------|----------|---------|---------|-----------|
| Age (years)       |          | 19      | 41      | 27.48±3.96 |
| Gravida           |          | 1       | 6       | 2.26±1.14  |
| Para              |          | 0       | 5       | 1.12±1.09  |
| POG (weeks)       |          | 28      | 43      | 35.56±3.57 |
| BMI (kg/m²)       |          | 18      | 28      | 21.67±1.45 |
| SBP               |          | 130     | 200     | 160.82±16.85 |
| DBP               |          | 90      | 130     | 102.19±9.28 |

**Newborn**

| Birth weight (g)  |          | 500     | 3840    | 2199.47±705.96 |
| APGAR 1 min       |          | 0       | 8       | 5.43±2.46   |
| APGAR 5 min       |          | 0       | 9       | 7.10±3.15   |

**Table 2: Characteristics in subgroups of hypertensive disorders of pregnancy**

| Parameter                      | GH (n=28) | CH (n=6) | PE (n=53) | E (n=33) | F | P   |
|--------------------------------|-----------|----------|-----------|----------|---|-----|
| Maternal age (years) (n=120)   | 27.43 (2.74) | 32.33 (5.44) | 27.04 (3.85) | 27.36 (4.12) | 3.394753 | 0.020 |
| Maternal POG (weeks) (n=120)   | 37.30 (2.61) | 36.17 (2.26) | 35.41 (3.51) | 34.21 (3.97) | 4.206914 | 0.007 |
| Birth weight (g) (n=124)       | 2551.07 (615.35) | 2773.33 (525.57) | 2085.82 (716.65) | 1950.43 (669.21) | 5.966595 | 0.001 |
| APGAR 1 min (n=124)            | 6.29 (2.02) | 7.00 (0)  | 5.38 (2.42) | 4.54 (2.74)  | 3.707191 | 0.016 |
| APGAR 5 min (n=124)            | 8.14 (2.38) | 9.00 (0)  | 7.04 (3.06) | 6.15 (3.72)  | 3.201991 | 0.026 |

Figures are mean (SD). GH: Gestational hypertension, CH: Chronic hypertension, PE: Preeclampsia, E: Eclampsia, POG (weeks): Period of gestation at the time of delivery in weeks, SD: Standard deviation
WHO multicountry survey also reported that there was about three-fold increased risk of perinatal death in women with PE and five-fold in women with eclampsia.[22]

The overall incidence of stillbirths in our study was 12.9% which is similar to the observation of Sharma et al., Sachan et al., and Berhe et al. (13.7%, 16.9%, 10%, respectively).[17,18,21]

The increased risk of stillbirth among women with PIH is related with the effect of decreased uteroplacental blood flow and placental ischemia related to hypertensive disorders of pregnancy which compromises blood flow to the fetus.[23,24]

The reason of high perinatal mortality seen by us is explained by the fact that our hospital is a tertiary care center catering to the rural population of the area received mostly referred women with complications during antenatal period or delivery process from centers which are not well equipped. The limited access to health-care services, insufficient availability, suboptimal or unknown quality of health services, and high out-of-pocket expenditure is among the key health challenges responsible for adverse perinatal and maternal outcomes in India.[25]

The incidence of neonatal deaths was 4.6% and is almost the same as observed by others 3.2%–4.3%. In our study, a high rate of NICU admissions (53.7%), ventilator requirement (25%), and five neonatal deaths was seen in PE and E groups, as most of the neonates were preterm, had FGR, low birth weight, low 1 min APGAR indicating the adverse effects of eclampsia and PE on neonatal outcome.[26]

Overall, 56.7% women had preterm delivery which is much higher than 28.8% reported by Yadav et al.[28] Sixty two (50%) of newborn showed FGR which is more than what was reported by Kolluru et al.[17] indicating that these women reported to us are an advance stage of disease necessitating urgent intervention because of maternal or fetal indications.

APGAR <7 at 5 min was seen in 21 (16.9%) of our neonates which is almost the same as seen by others (Kolluru et al. [19.8%] and Adu-Bonsaffoh et al. [14.7%]) and is in contrast with the observations of Vats and Paul (24.5%).[29] APGAR at 5 min improved in both eclampsia and PE groups and was <7 in 10 (28.6%) and 9 (16.4%) neonates, respectively, which was statistically significant (P = 0.002, P = 0.001), indicating a good neonatal resuscitation expertise of our attending pediatricians.

Out of 124 newborn, 80 (64.5%) had low birth weight and is similar as reported by Sachan et al. (56.4%).[18] Newborn of PE and eclampsia group contributed maximum to the low birth weight outcome (P = 0.0014) and is same as reported by Sharma et al. (47%).[17] Our finding of eclampsia mothers having 2.84 times the odds of having low birth weight babies is almost the same as reported by Bridwell et al. (5 times the odds of having low birth weight in eclampsia).[20]

Women with HDP have uteroplacental insufficiency causing chronic or acute hypoxia, FGR, and low birth weight which is further complicated by prematurity thus resulting in increased NICU admissions. Need for NICU admission needed in 58 (53.7%) babies is in contrast to observations of Sachan et al. (20.3%).[18] Neonates requiring ventilator after birth were managed in NICU by attending pediatrician which are same as reported by Sharma et al. (19%) but much less as reported by Yadav et al (40%).[29]

Increased perinatal loss indirectly reflects the status of maternal health that has to be improved at primary and secondary care levels by screening for the HDP, improving diet with calcium supplementation, reaching early diagnosis and timely referral to specialized centers where multidisciplinary team and NICU are available.

Hence, need of the hour is upgrading the primary health care, setting up of health, and wellness clinics at primary level.[30] Furthermore, training the health professionals to do screening for HDP, access signs and symptoms, reach diagnosis early, and refer high-risk mothers to a specialist at secondary level. This can only be done by strict implementation of Ayushman Bharat Program recommendations.[31] It is also recommended that auditing of all the perinatal deaths should be done.

**Study limitations**

Being a tertiary care hospital receiving mostly referred cases from rural areas, observations of this study cannot be generalized.
Table 4: Distribution fetal outcome in subgroups of hypertensive disorders of pregnancy

| Parameter                      | GH (n=28) | CH (n=6) | PE (n=55) | E (n=35) | Total (n=124) | P     |
|--------------------------------|-----------|----------|-----------|----------|---------------|-------|
| Maturity (weeks)               |           |          |           |          |               |       |
| >37                            | 19 (67.9) [35.8] | 3 (50.0) [5.7] | 19 (34.5) [35.8] | 12 (34.3) [22.7] | 53 (42.7) [100] | 0.0066 |
| 34-36+6                        | 6 (21.4) [17.1] | 2 (33.3) [5.7] | 21 (38.2) [60.10] | 6 (17.1) [17.1] | 35 (28.2) [100] |       |
| <34                            | 3 (10.7) [8.3] | 1 (16.7) [2.8] | 15 (27.3) [41.7] | 17 (48.6) [47.2] | 36 (29.1) [100] |       |
| FGR                            |           |          |           |          |               |       |
| Yes                            | 12 (42.9) [19.4] | 1 (16.7) [1.6] | 34 (61.8) [54.8] | 15 (42.9) [24.2] | 62 (50.0) [100] | 0.0710 |
| No                             | 16 (57.1) [25.8] | 5 (83.3) [8.1] | 21 (38.2) [33.9] | 20 (57.1) [32.3] | 62 (50.0) [100] |       |
| APGAR 1 min                    |           |          |           |          |               |       |
| 0-3                            | 3 (10.7) [15.8] | -         | 8 (14.5) [42.1] | 8 (22.9) [42.1] | 19 (15.3) [100] | 0.0003 |
| 4-6                            | 2 (7.1) [5.3] | -         | 21 (38.2) [55.3] | 15 (42.8) [39.5] | 38 (30.7) [100] |       |
| 7-10                           | 23 (82.1) [34.3] | 6 (100) [8.9] | 26 (47.3) [38.8] | 12 (34.2) [17.9] | 67 (54.0) [100] |       |
| APGAR 5 min                    |           |          |           |          |               |       |
| 0-3                            | 2 (7.1) [10.5] | -         | 8 (15.1) [42.1] | 9 (24.2) [47.4] | 19 (15.3) [100] | 0.2277 |
| 4-6                            | -         | 1 (3.8) [50] | 6 (21.4) [12.0] | 2 (1.6) [100] |       |       |
| 7-10                           | 26 (92.9) [25.2] | 6 (100) [5.8] | 46 (83.6) [44.7] | 25 (71.4) [24.3] | 103 (83.1) [100] |       |
| Birth weight (g)               |           |          |           |          |               |       |
| >2500                          | 19 (67.8) [43.2] | 4 (66.7) [9.1] | 14 (25.4) [31.8] | 7 (20.0) [15.9] | 44 (35.5) [100] | 0.0014 |
| 1500-2499                      | 8 (28.6) [14.3] | 2 (33.3) [3.6] | 28 (50.9) [50] | 18 (51.4) [32.1] | 56 (45.2) [100] |       |
| <1500                          | 1 (3.6) [4.2] | -         | 13 (23.7) [54.2] | 10 (28.6) [41.7] | 24 (19.3) [100] |       |
| NICU (n=108)                   |           |          |           |          |               |       |
| Yes                            | 7 (26.9) [12.1] | 3 (50.0) [5.2] | 26 (54.1) [44.8] | 22 (78.6) [37.9] | 58 (53.7) [100] | 0.0022 |
| No                             | 19 (73.1) [38.0] | 3 (50.0) [6.0] | 22 (45.9) [44.0] | 6 (21.4) [12.0] | 50 (46.3) [100] |       |
| Ventilator (n=108)             |           |          |           |          |               |       |
| Yes                            | 2 (7.7) [7.4] | 3 (50.0) [11.1] | 9 (18.7) [33.3] | 13 (46.4) [48.2] | 27 (25.0) [100] | 0.0028 |
| No                             | 24 (92.3) [29.6] | 3 (50.0) [3.7] | 39 (81.3) [48.2] | 15 (53.6) [18.5] | 81 (75.0) [100] |       |
| Stillbirths                    |           |          |           |          |               |       |
| Yes                            | 2 (7.1) [12.4] | -         | 7 (12.7) [43.8] | 7 (20.0) [43.8] | 16 (12.9) [100] | 0.3496 |
| No                             | 26 (92.9) [24.1] | 6 (100) [5.6] | 48 (87.3) [44.4] | 28 (80.0) [25.9] | 108 (87.1) [100] |       |
| Perinatal mortality            |           |          |           |          |               |       |
| Yes                            | 2 (7.1) [9.5] | -         | 9 (16.4) [42.9] | 10 (28.6) [47.6] | 21 (16.9) [100] | 0.0891 |
| No                             | 26 (92.9) [25.2] | 6 (100) [5.8] | 46 (83.6) [44.7] | 25 (71.4) [24.3] | 103 (83.1) [100] |       |

Early neonatal death was death of a liveborn neonate during the first 7 days after birth=5/108

Neonatal deaths

|       | Yes | No |
|-------|-----|----|
| GH    |     |    |
| CH    |     |    |
| PE    |     |    |
| E     |     |    |

Table 5: Odds ratio and 95% confidence interval in subgroups of hypertensive disorders of pregnancy

| Parameter          | GH     | CH     | PE     | E      |
|--------------------|--------|--------|--------|--------|
| Gravidity          | 1.23   | 0.34   | 1.12   | 0.86   |
| POG*               | 0.26   | 0.75   | 2.00   | 1.49   |
| AGPAR 1 min**      | 0.18   | -      | 1.63   | 3.10   |
| Low birth weight   | 0.17   | 0.25   | 2.25   | 2.84   |
| NICU (n=108)       | 0.22   | 0.85   | 1.03   | 4.48   |
| Ventilator (n=108) | 0.20   | 3.25   | 0.54   | 4.09   |
| FGR                | 0.69   | 0.18   | 2.37   | 0.67   |

Categorization: *POG: <37 and ≥37, **APGAR 1 m: <7 and ≥7. GH: Gestational hypertension, CH: Chronic hypertension, PE: Preeclampsia, E: Eclampsia, FGR: Fetal growth restriction, NICU: Neonatal intensive care unit, HDP: Hypertensive disorders of pregnancy

Figure are number (% in column) [% in row]. APGAR 1 min versus 5 min: GH: P=0.2762 nonsignificant, PE: P=0.001 significant, E: P=0.002 significant. GH: Gestational hypertension, CH: Chronic hypertension, PE: Preeclampsia, E: Eclampsia, FGR: Fetal growth restriction, NICU: Neonatal intensive care unit, HDP: Hypertensive disorders of pregnancy

to the remaining population. Results from a study done in one region cannot be applied to the other areas of the country because of different socioeconomic and cultural characteristics, and so, a multicenter trial from rural and urban population is required.
CONCLUSION

We observed that gestational hypertension, PE, and eclampsia were more common than CH and most of the perinatal deaths (90.5%) occurred in women having PE and eclampsia. Fetal growth restriction, prematurity, low birth weight, and low 1 min APGAR were the major contributors to perinatal deaths. We conclude that women with eclampsia and PE were associated with increased risk of adverse perinatal outcomes as compared to gestational and CH, necessitating vigilant antenatal care and timely management. Setting up of health and wellness clinics, upgrading primary and secondary health care, public awareness, and community involvement in understanding the need of regular antenatal care is most required.

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Conflicts of interest

There are no conflicts of interest.

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