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The Effect of Epidural Analgesia on Maternal and Early Neonatal Outcomes: A Retrospective Cohort Study in Qatar

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Abstract

Objective: Epidural Analgesia (EA) is commonly used method to alleviate labor pain. In the present study, we aimed to describe the maternal and neonatal morbidities associated with EA.

Methods: A retrospective cohort data analysis of the PEARL-Peristat Study. Our sample consisted of a total of 7721 singleton vaginal births occurred at the Woman's hospital between January 2017 and April 2018. Pregnancy characteristics and maternal and neonatal outcomes were compared between the two groups. Regression analysis was constructed to identify factors associated with the use of EA.

Results: Out of the total participants, 2969 women (38.5%) received epidural analgesia (EA) during labor. Several maternal and pregnancy factors were significantly associated with the use of EA, including Qatari nationality (adjusted odds ratio (aOR) 1.31, 95% confidence interval (CI) 2.10 (1.81-2.44), $p<0.001$), low parity (aOR 0.79 (0.66-0.96), $p=0.017$), vaginal birth after Cesarean (aOR 1.92 (1.51-2.45), $p<0.001$), labor induction (aOR 1.60 (1.39-1.85), $p<0.001$), prolonged first stage of labor (aOR 1.01 (1.01-1.02), $p<0.001$), and prolonged second stage of labor (aOR 1.01 (1.01-1.02), $p<0.001$). Among maternal and neonatal outcome variables, intrapartum fever (aOR 4.43 (1.47-13.38), $p=0.008$), instrumental delivery (aOR 4.43 (1.47-13.38), $p=0.003$), and reduced risk of meconium stained amniotic fluid (aOR 0.74 (0.55-0.99), $p=0.040$) were significantly associated with EA use during labor.

Conclusion: The study identified key factors associated with EA use during labor, including nationality, parity, birth type, labor stages, and specific maternal and neonatal outcomes. Further research is needed to better understand these associations and optimize EA use in labor management.

Keywords: Epidural Analgesia; Labour; Nulliparous; Qatari; Outcome; Neonate; Pregnancy

Introduction

Epidural Analgesia (EA), is a type of Neuroaxial Analgesia (NA) currently used by obstetricians to effectively reduce labor pain [1]. In recent years, the use of EA has increased significantly, with estimates ranging from 20–70% of all deliveries [2-6]. Absolute contraindications to NA are infrequent, while relative contraindications encompass coagulopathy, lower back infection, and increased intracranial pressure associated with intracranial pathology. Compared to parenteral opioids, EA provides significantly more analgesia, as measured by a visual analog scale in both the first and second stages of

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labour [7]. There is continuing controversy over whether EA impedes the progress of labor by causing dystocia and increasing the operative delivery rate, despite the association of NA with the reduction of anesthesia-related maternal mortality [8-10]. Several studies have described various adverse effects among pregnant women users of EA, such as a rise in body temperature, difficulty in the onset of lactation, hypotension, the prolonged second stage of labor, and an increase in instrumental vaginal delivery [1,6,11-15]. In some studies, EA has been suggested to potentially influence neonatal outcomes, leading to low Apgar scores and decreased umbilical arterial pH values. However, systematic reviews have not established a connection between the utilization of EA and an increase in Neonatal Morbidity [NM] [1,6,7,16-18]. Another recent findings indicate the impacts of NA on the risk of cesarean delivery, the length of labor, breastfeeding success, and pre-existing or new-onset low back pain have been largely reassuring [19]. In light of the conflicting research results concerning the outcomes of EA during labor, the primary objective of this study is to describe the maternal and neonatal morbidities associated with EA.

Methods

Study design

This was a retrospective cohort data analysis of the PEARL-Peristat Study data [Perinatal Neonatal Outcomes Research Study in the Arabian Gulf] Qatar. The PEARL-Peristat Study was a registry-based study designed to study immediate and long-term pregnancy outcomes of births using routinely collected hospital data. The study was funded by Qatar National Research Fund [Grant no. NPRP 6-238-3-059] and sponsored by the Medical Research Centre, Hamad Medical Corporation (HMC). The study was approved by the HMC Institutional Review Board [IRB], with a waiver of consent [HMC-IRB 13064/13].

Setting and participants

The sample for this study comprised of births from January 2017 and April 2018 conducted at the Women's Hospital [WH] [now known as the Women's Wellness and Research Center (WWRC)], in Qatar. As the largest governmental-operated tertiary hospital, this sample is generally representative of most births in the country. For this study, we retrieved 20625 singleton vaginal births from 24 weeks gestation and above. We then excluded babies with major congenital abnormalities, stillbirths, immediate neonatal death in the labor room or operating theatre, birth weights <2500g or >4000g, gestational age <37 weeks or >41+6 weeks, women with diabetes and hypertension, precipitate labor (defined as total labor duration less than 180 minutes, and other missing data [20]. We, therefore, analyzed 7721 births after exclusion as described above.

Comparison group

Women who received EA were compared to women without EA in labor.

Covariates and outcomes

Maternal: Explanatory factors included maternal age, parity grouped into nulliparous or greater than or equal to one parous experience and nationality was grouped into Qatari and no-Qatari. In addition, we examined the use of opioid analgesia [morphine] in labor and calculated the Body Mass Index [BMI] at delivery. Maternal outcomes studied included suspected chorioamnionitis, meconium-stained amniotic fluid [MSAF], labor duration [first stage, second stage, and third stage], instrumental delivery using vacuum or forceps, postpartum hemorrhage and admission to intensive care unit.

Newborn: These included Gestational Age (GA), Birth Weight (BW) and gender. Immediate outcomes included arterial and venous cord PH, Apgar score less than 7 at 1 and 5 minutes, admission to the Neonatal Intensive Care [NICU]. In addition, NICU admission reason such as respiratory distress and suspected sepsis. Other variables were birth trauma and in-hospital mortality. Birth trauma included caput succedaneum, subgaleal hematoma, cephalohematoma, brachial plexus injury, clavicular fracture, facial nerve injuries, and subconjunctival hemorrhage.

Statistical analysis

We summarized the distribution of variables using numbers and percentages, mean and standard deviation or median and interquartile ranges as appropriate. Based on the data type, we compared the proportions and the incidence of the study covariates and outcomes between the EA and control groups using either chi-square tests, Fishers' test or Mann-Whitney U test. Both univariate and multivariate logistic regression analyses were performed to account for potential confounding variables associated with EA. Statistical analysis was performed using IBM SPSS 26 [SPSS Inc., Chicago, IL, USA] statistical software with statistical significance set at $p<0.05$.

Results

The study group comprised 7721 nulliparous and multiparous women, 2969 women received EA (38.45%) while 4752 women did not received EA.

Table 1 shows the comparison of socio-demographic variables between the 2 groups. Mother received EA were younger in age than those who did not receive EA, also use of Opioid analgesia was significantly lower in the EA group [$p < 0.001$]. BMI was higher in EA group, nulliparous and Qatari women were more prevalent to receive EA [$p<0.001$]. Conversely, the proportion of multiparous women who received EA was significantly lower ($p < 0.001$).

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Table 1: Maternal demographic variables of both groups.

Epidural Analgesia							
	Total		No		Yes		p-value
	[n=7721]		[n=4752]		[n=2969]		
	n	%	n	%	n	%	
Maternal age*	28.12 ± 5.22		28.44 ± 5.25		27.61 ± 5.14		<0.001
BMI at delivery*	30.26 ± 5.14		30 ± 5.09		30.68 ± 5.2		<0.001
Parity							<0.001
Nullipara	2450	0.317	1074	0.226	1376	0.463	
Parity ≥1	5271	0.683	3678	0.774	1593	0.537	
Nationality							<0.001
Non-Qatari	5317	0.689	3471	0.73	1846	0.622	
Qatari	2404	0.311	1281	0.27	1123	0.378	
Opioid analgesia							<0.001
No	6100	0.79	3414	0.718	2686	0.905	
Yes	1621	0.21	1338	0.282	283	0.095	
*Values are expressed as “Mean ± SD”							

Table 2: Pregnancy Outcomes in both groups.

Epidural Analgesia							
	Total		No		Yes		p-value
	[n=7721]		[n=4752]		[n=2969]		
	n	%	n	%	n	%	
Intrapartum fever							
No	7602	0.985	4725	0.994	2877	0.969	
Yes	119	0.015	27	0.006	92	0.031	<0.001
VBAC							
No	7160	0.927	4443	0.935	2717	0.915	
Yes	561	0.073	309	0.065	252	0.085	0.001
Clinical chorioamnionitis							
No	7620	0.987	4726	0.995	2894	0.975	
Yes	101	0.013	26	0.005	75	0.025	<0.001
Membrane rupture[a]							
<18hrs	7071	0.918	4479	0.944	2592	0.876	
≥18hrs	631	0.082	265	0.056	366	0.124	<0.001
MSAF							
No	6504	0.843	4040	0.851	2464	0.83	
Yes	1209	0.157	706	0.149	503	0.17	0.015
Instrumental Delivery							
No	6999	0.906	4539	0.955	2460	0.829	
Yes	722	0.094	213	0.045	509	0.171	<0.001
PPH							
No	7323	0.948	4593	0.967	2730	0.92	
Yes	398	0.052	159	0.033	239	0.08	<0.001
1st stage of labor [mins] [a]	300 [230-386]		270 [220-345]		345 [270-448]		<0.001
2nd stage of labor [mins] [a]	15 [6-48]		10 [5-22]		43 [15-112]		<0.001
3rd stage of labor [mins] [a]	5 [5-7]		6 [5-8]		5 [5-7]		<0.001
Total labor duration [mins] [a]	330 [255-445]		295 [237 - 375]		415 [320-540]		<0.001
a =Missing data: membrane rupture [n=19], 1st stage of labor [n= 9], 2nd stage of labor [n=55], 3rd stage of labor [n=100], total duration of labor [n=2]. Labor data reported in median and interquartile range [IQR], VBAC; vaginal birth after caesarean, MSAF; meconium stained amniotic fluid, PPH; postpartum hemorrhage							

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Table 2 presents a comparison of maternal clinical outcomes between the two groups. The outcome measures include intrapartum fever, VBAC [vaginal birth after cesarean], chorioamnionitis, amniotic membrane rupture ≥ 18 hr [PROM] before one of birth, instrumental delivery, PPH [post-partum hemorrhage], and MSAF occurred significantly more frequently in mothers who received EA compared to those in the control group. Additionally, different stages of labor were compared between the two groups, the first and second stages, in addition to the total duration of labor (mins) were all prolonged in the EA group compared to the control group, however, the duration of the second stage of labor was shorter in the EA group.

Neonatal clinical characteristics and outcomes are presented in Table 3, many variables were higher in the EA group [p<0.001, <0.005] like GA, total NICU admission rates, birth trauma, NICU admission for suspected sepsis [p<0.001], and respiratory distress is higher in the EA [p=0.003]. Cord venous and arterial pH is lower in the EA [p<0.001and p<0.002]. There was no statistical difference between both groups in Apgar < 7 at 1 min and at 5 min [p=0.686 and p= 0.636]. No statistical difference was observed between both groups in BW [p=0.067] and gender [p=0.565]. There were no differences in later neonatal mortalities between the two groups.

To identify factors associated with EA, both univariate and multivariate logistic regression analyses were performed to

Table 3: Neonatal clinical characteristics and outcomes in both groups.

Epidural Analgesia							
	Total		No		Yes		p-value
	[n=7721]		[n=4752]		[n=2969]		
	n	%	n	%	n	%	
Birth weight*	3252.3 ± 343.9		3246.6 ± 341.5		3261.4 ± 347.8		0.067
Gestational age*	39.20 ± 1.08		39.16 ± 1.07		39.25 ± 1.10		<0.001
Cord arterial pH [a]*	7.29	0.1	7.29	0.1	7.28	0.09	0.002
Cord venous pH [a]*	7.32	0.09	7.33	0.09	7.31	0.08	<0.001
NICU admission							
No	7357	0.953	4581	0.964	2776	0.935	
Yes	364	0.047	171	0.036	193	0.065	<0.001
NICU admission for suspected sepsis							
No	7506	0.972	4662	0.981	2844	0.958	
Yes	215	0.028	90	0.019	125	0.042	<0.001
NICU admission for respiratory distress							
No	7623	0.987	4706	0.99	2917	0.982	
Yes	98	0.013	46	0.01	52	0.018	0.003
Gender							
Male	3887	0.503	2380	0.501	1507	0.508	
Female	3834	0.497	2372	0.499	1462	0.492	0.565
Apgar <7 at 1min							
No	7665	0.993	4719	0.993	2946	0.992	
Yes	56	0.007	33	0.007	23	0.008	0.686
Apgar <7 at 5mins							
No	7716	0.999	4749	0.999	2967	0.999	
Yes	5	0.001	3	0.001	2	0.001	0.636
Birth Trauma							
No	7658	0.992	4724	0.994	2934	0.988	
Yes	63	0.008	28	0.006	35	0.012	0.005
Newborn Outcome							
Discharged alive	7717	0.999	4748	0.999	2969	1	
In-hospital mortality	4	0.001	4	0.001	0	0	NA

a = Missing data: Cord arterial pH [n=6551], cord venous pH [n= 6605]
*Data reported as mean and SD. NA= not applicable

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account for potential confounding variables. These variables included maternal and pregnancy factors, as well as maternal and neonatal outcomes (Table 4). Maternal and pregnancy factors included maternal age, conception mode (artificial vs. natural), nationality, VBAC, parity, baby gender, gestational age, PROM, labor stages duration, labor induction using prostaglandin, maternal weight, height, and BMI at delivery.

After adjusting for these variables, Qatari nationality (adjusted odds ratio (aOR) 1.31, 95% CI 2.10 (1.81-2.44), $p<0.001$), parity (aOR 0.79 (0.66-0.96), $p=0.017$), VBAC (adjusted OR 1.92 (1.51-2.45), $p<0.001$), labor induction (aOR 1.60 (1.39-1.85), $p<0.001$), prolonged first stage of labor (aOR 1.01 (1.01-1.02), $p<0.001$), and prolonged second stage of labor (aOR 1.01 (1.01-1.02), $p<0.001$) were significantly associated with EA. Maternal and neonatal outcome variables (Table 4) included postpartum hemorrhage, chorioamnionitis, intrapartum fever, instrumental delivery, MSAF, cord arterial pH and base-deficits, low Apgar score at 1 minute, birth trauma, and NICU admission for respiratory distress or sepsis. After adjusting for other variables, the study found that intrapartum fever (aOR 4.43 (1.47-13.38), $p=0.008$), instrumental delivery (aOR 4.43 (1.47-13.38), $p=0.003$), and less risk of MSAF (aOR 0.74 (0.55-0.99), $p=0.040$) were significantly associated with EA during labor.

Table 4: Regression analysis of variables associated with use of epidural analgesia during labor.

Maternal and pregnancy characteristics: Epidural vs. no epidural analgesia				
Variables	unadjusted OR (95%CI)	p-value	adjusted OR (95%CI)*	p-value
Maternal age	0.70 (0.60−0.82)	<0.001	0.99 (0.81−1.23)	0.988
Maternal weight at delivery	1.01 (1.01−1.02)	<0.001	1.02 (0.95−1.10)	0.532
Maternal BMI	1.03 (1.02−1.04)	<0.001	0.96 (0.80−1.15)	0.663
Maternal height	1.02 (1.01−1.03)	<0.001	0.99 (0.92−1.07)	0.895
Conception mode, ART	2.12 (1.42−3.17)	<0.001	1.77 (0.98−3.18)	0.057
Nationality, Qatari	1.81 (1.63−2.02)	<0.001	2.10 (1.81−2.44)	<0.001
Parity	0.37 (0.34−0.42)	<0.001	0.79 (0.66−0.96)	0.017
VBAC	1.43 (1.18−1.73)	<0.001	1.92 (1.51−2.45)	<0.001
Membranes ruptured ≥18hr	2.16 (1.79−2.59)	<0.001	1.10 (0.82−1.47)	0.517
Labor induction	1.99 (1.76−2.25)	<0.001	1.60 (1.39−1.85)	<0.001
First stage of labor, duration	1.03 (1.02−1.03)	<0.001	1.01 (1.01−1.02)	<0.001
Second stage of labor, duration	1.02 (1.01−1.02)	<0.001	1.01 (1.01−1.02)	<0.001
Third stage of labor, duration	1.00 (0.99−1.02)	0.899	1.00 (0.99−1.01)	0.629
Gestational age	1.07 (1.02−1.12)	0.003	1.03 (0.96−1.10)	0.486
Birth weight	0.95 (0.99−1.00)	0.019	1.00 (0.99−1.00)	0.095
Female gender	0.94 (0.86−1.04)	0.263	0.90 (0.78−1.03)	0.136
Maternal and neonatal outcomes: Epidural vs. no epidural analgesia				
Variables	unadjusted OR (95%CI)	p-value	adjusted OR (95%CI)#	p-value
PPH	1.92 (1.55 −2.39)	<0.001	1.06 (0.67−1.67)	0.807
Chorioamnionitits	2.85 (1.82 −4.45)	<0.001	0.52 (0.17−1.60)	0.253
Intrapartum fever	3.47 (2.26−5.32)	<0.001	4.43 (1.47−13.38)	0.008
Instrumental delivery	3.18 (2.67−3.77)	<0.001	1.63 (1.18−2.26)	0.003
MSAF	1.18 (1.03−1.35)	0.017	0.74 (0.55−0.99)	0.04
Cord arterial pH	0.37 (0.10−1.39)	0.142	0.87 (0.19−4.08)	0.863
Cord arterial based deficit	0.98 (0.96−1.01)	0.313	1.002 (0.97−1.03)	0.903
Low 1 minute Apgar score	2.91 (1.37−6.19)	0.005	2.29 (0.74−7.03)	0.149
Birth trauma	1.85 (1.05−3.26)	0.034	1.16 (0.40−3.32)	0.787
NICU for respiratory distress	1.67 (1.09 −2.57)	0.018	0.72 (0.29−1.74)	0.462
NICU for suspected sepsis	1.80 (1.34 −2.41)	<0.001	1.09 (0.47−2.51)	0.84

OR, odds ratio; CI, confidence interva; BMI, body mass index; ART, assisted reproductive technologies; VBC, vaginal birth after Cesarean; PPH, postpartum hemorrhage; MSAF, meconium stained amniotic fluid
*adjusted for other variables in material and pregnancy characteristics group
#adjusted for all other variables in maternal and neonatal outcomes group

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Discussion

For reducing pain during labor, EA appears to be effective in this aspect. Due to conflicting results in the literature about this particular topic, our study aimed to describe the maternal and neonatal morbidities associated with EA in a large tertiary care center where 38.5% of the participants received EA during labor. The results of our study indicate that several maternal, pregnancy, and neonatal factors were significantly associated with the use of EA during labor. The results of this study revealed that several maternal and pregnancy variables were significantly linked to the use of EA, including Qatari nationality, lower parity, VBAC, labor induction, prolonged first and second stages of labor. Additionally, intrapartum fever, instrumental delivery, and a reduced risk of MASF were also found to be associated with EA use. However, after controlling for confounding variables, the study did not identify independent associations between certain outcomes such as birth trauma, low cord pH, low Apgar scores, or NICU admission for sepsis, chorioamnionitis, or respiratory distress and the use of EA in labor. This suggests that these outcomes may be influenced by other factors that are not related to EA use. In concordance with our study, one study compared the two groups in terms of socio-demographic data, the duration of the second stage of labor was prolonged in women received EA [33.13 ± 12.78 min], as compared to the control [27.53 ± 11.73 min]. On the contrary, the same study showed that the first stage of labor was shorter in the EA [4.83 ± 1.59 h] compared to the control group [5.48 ±1.56 h], and instrumental vaginal or cesarean delivery rates did not increase in patients received EA [21]. Another study found that EA and prolonged second stage of labor duration are not related to the neonatal morbidity, while the instrumental delivery doubles the risk of neonatal morbidity compared to the normal vaginal delivery. The authors therefore concluded that the second stage of labor does not need to be terminated for the duration alone [22,23]. Recent studies suggested that, although the duration of the second stage of labor is associated with increased risks of certain adverse maternal outcomes, there is no relationship between the duration of the second stage and adverse neonatal outcomes. However, most studies on this issue are from single centers [24-26]. For another aspect, one study showed that EA increases NICU admission, antibiotic exposure, neonatal birth injuries, need for positive pressure ventilation at birth, and respiratory distress in the first 24 hours of life. Moreover, mothers who received EA, had a longer second stage, temperature elevation >37.5°C, and subjected to more instrumental delivery [6,27]. A recent study from Qatar showed similar findings to ours with regards to EA being related to a prolonged second stage of labor and increased rate of instrumental delivery. However, our study found a negative association to MSAF. Additionally, in this study, we did not observe an independent association between fetal distress, or birth trauma and EA [27]. Previous single-center studies have found conflicting results regarding the contribution of maternal EA to neonatal administration of antibiotics [28,29]. One of the major clinical criteria for sepsis evaluation is maternal intrapartum fever. However, EA can also lead to maternal fever and is not associated with an increased risk of infection in the neonate, thus leading to unnecessary neonatal exposure to antibiotics [30]. Among a large cohort of mother-neonate pairs across the state of Colorado over 6 years, EA was associated with a 26% increased odds of neonatal exposure to antibiotics. Although mothers who received EA were 5 times more likely to have a fever, the proportion of neonates treated with antibiotics did not differ by EA status. This result supports the hypothesis that EA is a risk factor for noninfectious maternal fevers, but neonates born to mothers with fever were treated without respect to whether the mother had an EA [31]. In other studies, it was found that EA is associated with increased rates of maternal intrapartum fever [29,32-34]. However, the relationship between EA, maternal fever, and neonatal antibiotic treatment has been limited to conflicting single-center studies at academic, and tertiary care institutions. Goetzl et al. [28] conducted a follow-up study of a cohort of 1934 births which demonstrated that in mothers with low grade [<37.5°C] or no fever, EA was associated with a three-fold increased risk of sepsis evaluation in neonates as well as increased rates of neonatal antibiotic treatment [28]. In contrast, Kaul et al. [29] found no association between EA and neonatal sepsis evaluation in 1177 primiparous births at Magee-Women's Hospital, Pittsburg, Pennsylvania, USA [29]. Our results showed that cord venous and arterial pH values were lower in the EA group. However, no statistically significant associations were observed between cord pH values and EA after controlling for other variables, similar to low Apgar scores at 1 minute and 5 minutes. This finding is consistent with several previous studies that found no significant differences in neonatal outcomes between the EA and control groups [7,21,27,35-37]. In a Cochrane review by Anim-Somuah et al. [28], EA did not appear to have an immediate effect on neonatal status as determined by the Apgar score, with an OR of 0.70 [, 95% CI 0.44–1.10] for an Apgar score of < 7 after EA [28]. However, other studies reported a higher incidence of low Apgar score in the EA group and higher needs for neonatal resuscitation among women who received EA [29,37,38].

Conclusion

The study showed that several maternal and pregnancy variables, such as Qatari nationality, lower parity, VBAC, labor induction, and prolonged first and second stages of labor, were significantly related to the use of EA. Additionally, maternal and neonatal outcomes variables, such as intrapartum fever, instrumental delivery, and reduced risk of MASF, were also found to be associated with EA use. However, the study did

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not find independent associations between certain outcomes, such as birth trauma, low cord pH, low Apgar scores, or NICU admission for sepsis or respiratory distress, and the use of EA in labor. This highlights the need for obstetricians to provide balanced and comprehensive information on EA to pregnant women considering this option. Given the limited information on the effect of opioid analgesia on labor pain in association with EA, it may be beneficial to conduct further studies in this area.

The study's limitations include its retrospective design, which may introduce selection bias, and the potential for unmeasured confounding factors. Additionally, the single-center setting may limit the generalizability of the findings to other populations. Furthermore, some data points were missing for certain variables, which may impact the analysis and conclusions. The study also focuses on short-term outcomes, limiting its ability to assess long-term effects. Lastly, the presence of other confounding variables not accounted for in the study may influence the observed associations.

Conflict of iInterest

Each author declares that he or she has no commercial associations [e.g. consultancies, stock ownership, equity interest, patent/licensing arrangement etc.], that might pose a conflict of interest in connection with the submitted article.

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