Original Article

Prevalence and Factors Associated with Neonatal Sepsis in a Tertiary Hospital, North West Nigeria

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Abstract

Context: Neonatal sepsis is an important cause of morbidity and mortality of newborns, especially in developing countries. **Aims:** Our study determined the prevalence of neonatal sepsis and its predisposing factors among neonates admitted in Ahmadu Bello University Teaching Hospital (ABUTH). **Settings and Design:** This was a cross-sectional descriptive study conducted in ABUTH. **Subjects and Methods:** The data were abstracted from the case notes of neonates admitted from May 2017 to May 2018. A pretested pro forma was used to abstract the data. **Statistical Analysis Used:** Odds ratios and multivariate logistic regression were used to determine the factors associated with neonatal sepsis among the study population. **Results:** The prevalence of neonatal sepsis was 37.6%. *Escherichia coli* was the most commonly isolated organism. Neonates 0–7 days of age were 2.8 times less likely to develop neonatal sepsis than older neonates. Babies born with an Apgar score of <6 within the 1st min were 2.4 times more likely to develop neonatal sepsis than those whose Apgar score was higher. Neonates of mothers who had urinary tract infection during pregnancy were 2.3 times more likely to have had sepsis and those whose mothers had premature rupture of membranes were 4.6 times more likely. **Conclusions:** The prevalence of neonatal sepsis was high among the neonates studied. Neonatal and maternal factors were associated with sepsis in the neonates. These findings provide guidelines for the selection of empirical antimicrobial agents in the study site and suggest that a continued periodic evaluation is needed to anticipate the development of neonatal sepsis among neonates admitted.

Keywords: Empirical antimicrobials, neonatal, predictors, septicemia, tertiary

Introduction

Neonatal sepsis is a clinical syndrome characterized by systemic signs of circulatory collapse, caused by the invasion of the blood stream by bacteria in the first 28 days after birth.[1] It is caused by both Gram-positive and Gram-negative bacteria.[2] It can present in several ways with a substantial number of cases having nonspecific signs and symptoms at presentation. The salient clinical features include systemic signs of infection such as fever, hypothermia, tachycardia, failure to thrive, lethargy, irritability, listlessness, as well as isolation of a bacterial pathogen from the bloodstream.[3] It is an important cause of morbidity and mortality in the neonatal period.[4] It is also one of the leading causes of mortality in the first 28 days after birth both in the developed and developing parts of the world.[5] This is so because neonates (especially preterms) produce immunoglobulins at a lower rate when compared to adults, thus making them susceptible to infections due to this "impaired immunity."[6]

Access this article online

Quick Response Code:

Website: www.nigeriamedj.com

DOI: 10.4103/nmj.NMJ_31_19

Neonatal sepsis can be broadly classified into two subtypes depending on the time of onset of symptoms: early onset if the onset of symptoms is 72 h or less after birth which is usually caused by organisms associated with female genital tract and late onset if greater than 72 h after birth.[7] The risk factors for the early onset include prematurity, low birth weight, chorioamnionitis, maternal febrile illnesses, and prolonged rupture of membranes (PROM).[8,9] However, late-onset neonatal sepsis is caused by the organisms associated with the environment and may be nosocomial in origin. The risk factors

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Submitted: 04-Mar-2019 **Revised:** 03-Sep-2019
Accepted: 26-Oct-2019 **Published:** 07-May-2020

How to cite this article: Olorukooba AA, Ifusemu WR, Ibrahim MS, Jibril MB, Amadu L, Lawal BB. Prevalence and factors associated with neonatal sepsis in a tertiary hospital, North West Nigeria. Niger Med J 2020;61:60-6.

for late-onset neonatal sepsis are invasive procedures such as resuscitation in the delivery room, intubation, mechanical ventilation, central venous catheters, surgical procedures, and staying in neonatal intensive care unit for prolonged period of time. Furthermore, the use of broad-spectrum antibiotics is a risk factor for fungal neonatal sepsis.[8]

There is a high prevalence of neonatal sepsis in Nigeria, with neonatal blood culture-positive rates ranging from 25% to 55% reported in various studies carried out in Nigeria.[10] Neonatal sepsis has been associated with high morbidity and mortality;[11] thus, failure to promptly diagnose and treat could lead to high mortality.[12] In Nigeria, sepsis-related case fatality rates ranged from 26.7% in Abakaliki to 27.3% in Jos and 33.3% in Ile-Ife over the past two decades.[13] Sepsis during the neonatal period can lead to various complications. The short-term complications include respiratory failure, pulmonary hypertension, cardiac failure, shock, renal failure, liver dysfunction, and cerebral edema.[14] Some long-term complications include developmental delays and sensory and neurological dysfunction.[14]

The assessment of the prevalence, clinical outcomes, and risk factors for neonatal sepsis among neonates in a tertiary facility will help provide information to policymakers and/or management to take more preventive measures in reducing the risk among neonates. Furthermore, the knowledge of pathogens causing infections in young infants is essential for designing hospital-based management strategies. This study was carried out to determine the prevalence of neonatal sepsis and to identify the associated predisposing factors as well as the bacteriological profile of neonatal septicemia in the Special Care Baby Unit (SCBU) of Ahmadu Bello University Teaching Hospital (ABUTH), Nigeria.

Subjects and Methods

ABUTH is located in Zaria, North-western Nigeria, and serves as a referral and regional intensive care center.

The SCBU has 22 beds, of which 14 for the inborn neonates and 8 for the outborn neonates.

This study employed a cross-sectional design involving review of the case notes of all neonates and their laboratory records to assess the prevalence and risk factors for neonatal sepsis during this period.

The Fisher's formula was used to estimate the minimum sample size for the study.[15] Taking the prevalence of neonatal sepsis from a previous study as 41.2%,[16] standard normal deviate at 95% confidence interval as 1.96, margin of error as 5%, and nonresponse rate of 10%, the minimum sample size estimated was 409. Thus, the data were extracted from the case notes of all neonates admitted during the period under review.

A pro forma adapted from the previous studies[4,10,11] was used to collect the information from the case notes of all babies admitted over a period of 2 months (July and August 2018). The pro forma had two sections (A and B). The first section collected information on maternal characteristics of the neonate, such as mother's age, parity, and occupation, whereas the second section was used to collect neonatal characteristics such as age (in days), sex, and birth weight. The pro forma was first pretested with forty case notes of neonates who were in the SCBU in April 2018. Data collection was done using Open Data Kit collect software version v1.13.2 (ODK development team, UW, USA) installed in an android device, containing the pro forma.

The data obtained were extracted from the android device and were analyzed using the STATA software version 13.0 (StataCorp, College Station, TX, USA). A neonate with septicemia was identified as anyone with a proven or suspected infection in the presence of at least two of the following laboratory findings:[17] white blood cell count <4000 × 10^9 cells/l or more than 20,000 ×10^9 cells/l, ratio of immature white blood cells to total neutrophil >0.2, platelet count <100,000 × 10^9 cells/l, C-reactive protein more than 15 mg/l or procalcitonin that was 2 ng/ml or higher, glucose intolerance confirmed at least two times with blood glucose more than 180 mg/dl or 10 mMol/l or blood glucose <45 mg/dl or 2.5 mMol/l despite receiving age-specific normal range glucose amounts, and metabolic acidosis with base excess of <10 mEq/l or with serum lactate more than 2 mMol/l.

The results were represented using frequencies and simple percentages to describe the categorical variables. The Chi-square and Fisher's exact tests were used to test for association between neonatal sepsis and various maternal and neonatal characteristics with statistical significance set at $P < 0.05$. Stepwise logistic regression was used to determine the predictors of neonatal sepsis.

Ethical approval for the research was obtained from the Ethics and Scientific Committee of ABUTH, Zaria. Permission to conduct the study was obtained from the head of the Records Unit, ABUTH. For confidentiality, the patient's names were not included in the collection form. Only the investigator had access to the laboratory records and medical files for the purposes of the study. The data collected were stored in a laptop with a password. Only the researchers had access to this laptop.

Results

Four hundred and sixty-five case notes were reviewed in the SCBU of ABUTH during the period of the study. Of these, 175 (37.6%) had neonatal sepsis.

The mean age ± standard deviation of the mothers was 27.9 ± 6.1 years [Table 1]. Only 2 (0.4%) of the mothers were above 45 years of age. About three-quarters (343; [73.8%]) were multiparous, whereas about one-third (171; [36.8%]) had tertiary level education. Spontaneous vaginal delivery was the most common method (325; [69.9%]) of delivery among them. Only 23 (5%) of the mothers did not attend antenatal care (ANC) during pregnancy and 69 (14.8%) had prolonged labor [Table 1].

More than half (55.1%) of the neonates were male [Table 2]. The median age (range) of neonates was 2 (0–26) days. About a quarter of the neonates (24.3%) were preterm, with majority (79.3%) having APGAR score of <7 in the 1st min. There were 96 (54.9%) males and 79 (45.1%) females, giving a male-to-female ratio of 1.2:1. Ninety-two (52.6%) neonates had birth weights >2.5 kg. Thirty-four (19.4%) neonates were preterm and 141 (80.6%) term neonates and no postterm had neonatal sepsis [Table 2].

Table 1: Characteristics of mothers of the neonates studied (*n*=465)

Characteristics	Frequency (%)
Mother's age (years)	
15-24	145 (31.2)
25-34	243 (52.3)
35-44	75 (16.1)
≥45	2 (0.4)
Mother's parity	
Primiparous	122 (26.2)
Multiparous	286 (61.5)
Grand multiparous	57 (12.3)
Mother's tribe	
Hausa/fulani	319 (68.6)
Others	146 (31.4)
Mother's occupation	
Unemployed	322 (69.2)
Employed	143 (30.8)
Mother's religion	
Islam	368 (79.1)
Christianity	97 (20.9)
Mother's education	
None	37 (8)
Arabic	7 (1.5)
Primary	118 (25.4)
Secondary	132 (28.4)
Tertiary	171 (36.8)
Mode of delivery	
Forceps	16 (3.4)
C-section	124 (26.7)
SVD	325 (69.9)
ANC attendance	
Yes	442 (95.1)
No	23 (5.0)
UTI during pregnancy	
Yes	54 (11.6)
No	411 (88.4)
PROM during pregnancy	
Yes	41 (8.8)
No	424 (91.2)
Prolonged labor	
Yes	69 (14.8)
No	396 (85.2)
Foul-smelling liquor	
Yes	32 (6.9)
No	433 (93.1)

SVD – Spontaneous vaginal delivery, UTI – Urinary tract infection, PROM – Prolonged rupture of membranes, ANC – Antenatal care

One hundred and seventy-five neonates had positive blood culture, giving a prevalence rate of blood culture-proven sepsis among the neonates as 37.6%. The most common (31.0%) organism that caused sepsis was *Escherichia coli* [Figure 1]. There were 93 (53.1%) neonates with early-onset sepsis (onset of illness within the first 72 h after birth). Neonates 0–7 days of age were 2.8 times less likely to develop neonatal sepsis than older neonates. Babies born with an Apgar score of <6 within

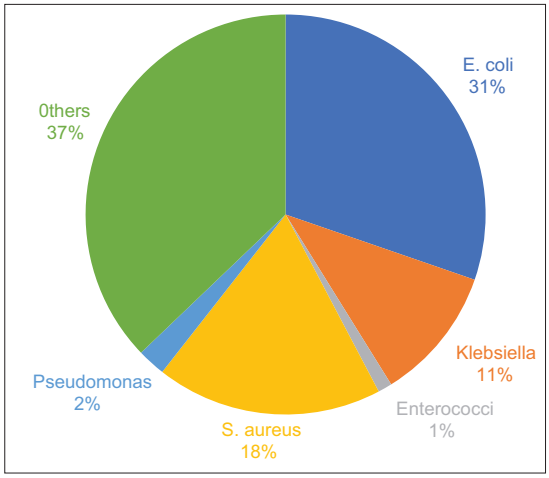

Figure 1: Causative organisms responsible for neonatal sepsis among study neonates in the Ahmadu Bello University Teaching Hospital

Table 2: Neonatal characteristics of the study population (*n*=465)

Characteristics	Frequency (%)
Age (days)	
0-7	408 (87.7)
8-28	57 (12.3)
Sex	
Male	256 (55.1)
Female	209 (44.9)
Birth weight (g)	
<2500	219 (47.1)
≥2500	246 (52.9)
Maturity (weeks)	
<37	113 (24.3)
≥37	352 (75.7)
Apgar score 1st min	
<3	295 (63.4)
4-6	74 (15.9)
≥7	96 (20.6)
Apgar score 5th min	
<3	260 (55.9)
4-6	66 (14.2)
≥7	139 (29.9)
Resuscitation	
Yes	180 (38.7)
No	285 (61.3)
Cried immediately	
Yes	339 (72.9)
No	126 (27.1)

Table 3: Predisposing factors to sepsis in neonates in the special care baby unit of the Ahmadu Bello University Teaching Hospital

Neonatal characteristics	Neonatal sepsis		COR	*P*	AOR	*P*
	Yes (%)	No (%)				
Age (days)						
0-7	137 (33.6)	271 (66.4)	3.956 (2.198-7.121)	<0.001	2.82 (0.192-0.651)	0.001
8-28	38 (66.7)	19 (33.3)	1			
Sex						
Male	96 (37.5)	160 (62.5)	0.947 (0.677-1.440)	0.947		
Female	79 (37.8)	130 (62.2)	1			
Birth weight (g)						
<2500	92 (42.0)	127 (58.0)	0.703 (0.482-1.024)	0.067		
≥2500	83 (33.7)	163 (66.3)	1			
Maturity (weeks)						
<37	34 (30.1)	79 (69.9)	0.644 (0.409-1.015)	0.058		
≥37	141 (40.1)	211 (59.9)				
Apgar score 1st min						
<6	157 (42.5)	212 (57.5)	3.209 (1.847-5.576)	<0.001	2.393 (1.071-5.348)	0.033
≥6	18 (18.8)	78 (81.3)	1			
Apgar score 5th min						
<6	143 (43.9)	183 (56.1)	0.383 (0.244-0.601)	<0.001		
≥6	32 (23.0)	107 (77.0)	1			
Resuscitation						
Yes	55 (30.6)	125 (69.4)	1.653 (1.114-2.453)	0.013		
No	112 (41.2)	160 (58.8)	1			
Cried immediately						
Yes	137 (40.4)	202 (59.6)	0.637 (0.411-0.987)	0.043		
No	35 (28.7)	87 (71.3)	1			

COR – Crude odds ratio, AOR – Adjusted odds ratio

the 1st min were 2.4 times more likely to develop neonatal sepsis than those whose Apgar score was higher [Table 3]. Neonates of mothers who had urinary tract infection (UTI) during pregnancy were 2.3 times more likely to have had sepsis and those whose mothers had PROM were 4.6 times more likely [Table 4].

Discussion

Neonatal morbidity and mortality are key public health challenges in our local setting, with an enormous percentage of deaths in the neonatal period attributable to sepsis. An estimated 98.5% of neonatal mortality occurs in developing countries, with neonatal sepsis unswervingly responsible for 26% of neonatal deaths.[18] Despite efforts to reduce neonatal mortality globally, in 2015, nearly half of the 5.9 million under-five deaths occurred in the neonatal period,[19] and 80% countries with the highest neonatal mortality rates are in Sub-Saharan Africa (SSA).[20]

This study aimed to assess the prevalence as well as maternal and neonatal risk factors of neonatal sepsis to contribute to tackle the burden of the illness and its related problems. The prevalence of neonatal sepsis in this study was found to be high (37.6%) with about three-fourth of these cases (78.2%) with early-onset neonatal sepsis (<7 days), which is to a certain extent comparable with other studies.[21,22] Many studies done around the world show the prevalence of neonatal sepsis differently; however, the prevalence of studies around SSA and other developing countries is higher than that of the developed countries.[23] The prevalence in our study is comparable with studies from different parts of the world:[24] a prevalence of 39% in New Delhi, India,[24] 45.9% in Egypt,[25] 38.9% at a tertiary hospital, Mwanza, Tanzania, [26] and 31.4% in Dar es Salaam.[27] Similar findings were also obtained in other Nigerian teaching hospitals: 33.1% in Olabisi Onabanjo University Teaching Hospital, Shagamu, South-western Nigeria.[13] A prevalence of 38.95% was seen from a study in University of Benin Teaching Hospital.[10] In University of Maiduguri Teaching Hospital, the prevalence was 42%.[11] In Jos University Teaching Hospital, the prevalence was 41.2%[16] and a study done in this hospital (ABUTH) in 2005 showed 35.5% prevalence.[9] However, other studies have revealed marked difference in the prevalence from our study: in Iraq 8.9%,[28] Mexico 4.3%,[7] Pokhara Nepal 69.05%,[29] Zambia 54%,[30] and Uganda 21.8%.[31] The reasons for these disparities could be alluded to the difference in hospital settings as it has been shown that neonatal sepsis is an issue in resource-poor settings.[32]

The pathogens most often implicated in neonatal sepsis in developing countries differ from those seen in developed countries. Overall, Gram-negative organisms are more common and are mainly represented by *Klebsiella, E. coli, Pseudomonas,* and *Salmonella*.[33-37] Of the Gram-positive

Table 4: Maternal predisposing factors to sepsis in neonates in the special care baby unit of the Ahmadu Bello University Teaching Hospital

Maternal characteristics	Neonatal Sepsis		COR	*P*	AOR	*P*
	Yes (%)	No (%)				
Mother's age (years)						
15-24	70 (48.3)	75 (51.7)	1.9 (1.090-3.459)	0.024		
25-34	80 (32.9)	163 (67.7)	1.0 (0.591-1.764)	0.941		
35 and above	25 (32.5)	52 (67.5)	1			
Mother's parity						
Primiparous	50 (41.0)	72 (59.0)	0.9 (0.505-1.807)	0.887		
Multiparous	101 (35.3)	185 (64.7)	0.7 (0.421-1.339)	0.332		
Grand multiparous	24 (42.1)	33 (57.9)	1			
Mother's tribe						
Hausa/fulani	134 (42.0)	185 (58.0)	0.5 (0.353-0.824)	0.004		
Others	41 (28.1)	105 (71.9)	1			
Mother's occupation						
Unemployed	135 (41.9)	187 (58.1)	0.5 (0.353-0.824)	0.004		
Employed	40 (28.0)	103 (72.0)	1			
Mother's religion						
Islam	148 (40.2)	220 (59.8)	0.6 (0.351-0.936)	0.026		
Christianity	27 (27.8)	70 (72.2)	1			
Mother's education						
None	17 (45.9)	20 (54.1)	7.4 (1.393-39.763)	0.019		
Arabic	5 (71.4)	2 (28.6)	2.5 (1.216-5.267)	0.013		
Primary	49 (41.5)	69 (58.5)	2.1 (1.278-3.497)	0.04		
Secondary	61 (46.2)	71 (53.8)	2.6 (1.573-4.159)	<0.001		
Tertiary	43 (25.1)	128 (74.9)	1			
Mode of delivery						
Assisted delivery	4 (25.0)	12 (75.0)	0.4 (0.209-1.294)	0.128		
C-section	25 (20.2)	99 (79.8)	0.3 (0.190-0.505)	<0.001		
SVD	146 (44.9)	179 (55.1)	1			
ANC attendance						
Yes	161 (36.4)	281 (63.6)	0.4 (0.156-0.870)	0.023		
No	14 (60.9)	9 (39.1)	1			
UTI during pregnancy						
Yes	32 (59.3)	22 (40.7)	2.7 (1.527-4.866)	0.001	2.3 (1.194-4.274)	0.012
No	143 (34.8)	268 (65.2)	1		1	
PROM						
Yes	28 (68.3)	13 (31.7)	4.1 (2.041-8.072)	<0.001	4.6 (2.156-9.719)	<0.001
No	147 (34.7)	277 (65.3)	1		1	
Prolonged labor						
Yes	26 (37.7)	43 (62.3)	0.3 (0.124-0.490)	<0.001		
No	149 (37.6)	247 (62.4)	1			
Foul-smelling liquor						
Yes	19 (59.4)	13 (40.6)	0.4 (0.185-0.801)	0.11		
No	156 (36.0)	227 (64.0)	1			

PROM – Premature rupture of membrane, COR – Crude odds ratio, AOR – Adjusted odds ratio, SVD – Spontaneous vaginal delivery, ANC – Antenatal care, UTI – Urinary tract infection

organisms, *Staphylococcus aureus*,[35,36,38] coagulase-negative staphylococci,[39] and *Streptococcus pneumoniae*[40] are the most commonly isolated. In our study, the most common isolated organisms causing neonatal sepsis were *E. coli* (31%), followed closely by *S. aureus* (18%). Other organisms also isolated included *Klebsiella*, *Enterococci,* as well as *Pseudomonas*. This finding is quite different from the findings from the same hospital (ABUTH) a decade ago, in which *S. aureus* (42.9%) was the most common, followed by *E. coli* (19.5%), *Streptococcus* species (11.0%), *Klebsiella pneumoniae* (7.8%), and *Proteus mirabilis* (6.5%).[9] This suggests a change in etiology over the years. In most studies done in Nigeria, *S. aureus* was found to be the most common causative agent. For example, Pius *et al*. in Maiduguri reported *S. aureus* to be responsible for about one-third of cases,[11] and Awoniy *et al*. in Ife reported almost the same

finding (28%).[41] In India, *Klebsiella* was reported to be the most common cause (48.21%), others being *S. aureus*, *E. coli*, *Enterococcus*, and methicilin-resistant *S. aureus*; [42] this is in contrast to what was found in this study. The observation of the organisms commonly associated with neonatal sepsis in this study will help in the choice empirical antibiotics for the management of neonatal sepsis before blood culture result becomes available. This is necessary for reducing the chances of complications that are associated with delay in commencing the definitive treatment for neonatal sepsis.[8]

In this study, the neonatal risk factors for sepsis identified were age and Apgar score at the 1st min after birth. Neonates who were 0–7 days of age were 2.8 times more likely to develop sepsis while those who had Apgar score <6 in the 1st min after birth were 2.4 times more likely. Previous studies have also reported age to be a risk factor for neonatal sepsis.[43,44] Similarly, previous studies have also found Apgar score to be an important risk factor for neonatal sepsis.[45] This finding could be helpful in guiding the management of neonates by ensuring that those with low Apgar score in the 1st min after birth are managed with strict sepsis preventive measures.

Maternal risk factors for neonatal sepsis found in this study were PROM and UTI during the index pregnancy. In this study, neonates born to mothers who had PROM during pregnancy were 4.6 times more likely to have developed sepsis. This is consistent with the finding in Soweto.[46] However, contrasting findings were observed in earlier studies conducted in different parts of the world.[9,44,47-49] Early rupture of membrane and prolonged labor increases the chance of ascending microorganisms from the birth canal into the amniotic sac and fetal compromise as well as asphyxia which frequently leads to sepsis in the neonatal period.[50] This finding could serve as justification for prophylactic antibiotic therapy for neonates born to mothers with a history of PROM during pregnancy.

In this study, about one-fifth of the neonates were born to mothers who had a history of UTI during the index pregnancy. Neonates born to mothers who had UTI during pregnancy were two times more likely to have developed sepsis, and this finding is comparable with the findings of previous studies conducted in Ghana and Ethiopia.[44,45] This finding is consistent with the assertion that maternal UTI is often associated with early-onset neonatal sepsis, especially if untreated during the third-trimester pregnancy or labor, and it may be associated with neonatal sepsis following the colonization of the birth canal by the infectious agent.[51]

Birth weight, mother's age, sex, gestational age, parity, ANC, prolonged labor, mother's occupation, mother's level of education, and foul-smelling liquor were not found to be predictors of neonatal sepsis in this study. This is contrary to the findings of other studies on risk factors of neonatal sepsis in different parts of the world, which indicated that these factors had an influence on neonatal sepsis.[27,29,30,44,51-55] The reasons for these differences, though unclear, may be related to facility-related factors. However, these factors were not assessed in this study.

Conclusion

The prevalence of neonatal sepsis was found to be high among the neonates studied. *E. coli* was the most commonly isolated organism. The risk factors for neonatal sepsis found were both maternal (PROM and UTI in pregnancy) and neonatal (Apgar score in the 1st min after birth and age). These findings provide guidelines for the selection of empirical antimicrobial agents in the study site and suggest that a continued periodic evaluation is needed to anticipate the development of neonatal sepsis among neonates admitted. Further research should be conducted to assess the influence of facility factors in the causation of neonatal sepsis.

Acknowledgments

The authors wish to acknowledge the Hospital's Medical record department for their permission to collect this data. Finally, we would like to acknowledge our friends who were very interested, encouraged, and helped us to do this research project.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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