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Prevalence of Hypomagnesaemia in Children Admitted to the Pediatric Intensive Care Unit and its Related Factors in Zahedan, Iran

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Abstract

Background: Clinical status of children admitted to the intensive care units (ICUs) is important. We aimed to investigate prevalence of hypomagnesaemia in children admitted to the pediatric intensive care unit (PICU), and its relation factors.

Materials and Methods: This cross-sectional study was conducted in Ali Ebne Abitalib Hospital Zahedan, Iran, in 2018. From total children who were admitted to the PICU, 150 individuals aged one month to 12 years that were entered to the study. Magnesium level was estimated by XYLIDYL BLUE method using Erba kits. Children were divided into two groups based on their serum magnesium concentration defined as normal and abnormal. Data were analyzed using SPSS software version 18.0.

Results: From 150 admitted children to the PICU, 44.7% were hypomagnesaemia with longer hospital stay, higher levels of Na, K and Ca ($p>0.05$). During the first five day of hospitalization, 58 children died, most of them were hypomagnesaemia. About 39.6% of 101 children who consumed diuretic medicine were hypomagnesemia. This pattern was 43.8% and 40.00% from 130 and 85 patients who used digital or aminoglycoside medicines. About half of the children who had heart diseases were hypomagnesemia. These trends were 33.3% in kidney and sepsis; about 50.00% and 43.5% were hypomagnesaemia from those who had central nervous disorder and respiratory problems, respectively. The eldest children had 1.79 times higher odds (95% CI=0.76 to 8.30) to be hypomagnesaemia compared to the youngest, and girls had 1.01 times higher odds (95% CI=0.44 to 2.30) to be hypomagnesaemia.

Conclusion: Prevalence of hypomagnesaemia in children admitted to the PICU was high and it was associated with the major electrolytes of sodium, potassium, and calcium.

Key Words: Hypomagnesaemia, Prevalence, Factors, PICU.

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1- INTRODUCTION

Assessing the effects of staying in pediatric intensive care unit (PICU) in children is critical due to high mortality rate and various morbidities (1). Abnormality in electrolytes such as sodium (Na), potassium (k), calcium (Ca), magnesium (Mg), and Phosphorus (P) are key factors that have to be considered in these children (2). These variations affect cell structures that caused disorder or mortality (3). Among these components, Mg is noticeable, with the prevalence of 10% to 15% and 60% in hospital and ICU patients, respectively (4). It has been reported that its disorder is frequently becoming worse due to clinical conditions such as protein–energy, malnutrition, mal-absorption, hypoalbuminaemia, sepsis and hypothermia, which are mostly observed in developing countries (5), and the disturbances are likely following prolonged gastrointestinal suctioning, blood transfusion, catecholamine excess, and aminoglycoside therapy (6).

Additionally, Mg plays a role in muscle utility including muscle tightening, protein synthesis, production of energy and liquid balance. Mg is a physiologic controller in cell covering reliability and contributes to the function of neuromuscular, cardiovascular, immunologic, and hormonal systems (7). Also, Mg has necessary roles in most cellular reaction as a cofactor in up to 300 metabolic reactions such as glycolysis, fat and protein metabolism and ATP synthesis (8). Mg is the fourth most abundant cation and the second most abundant intracellular cation in the human body. It is important in maintaining several cellular functions, as it is a natural activator of most enzymes. Less than 1% of total body Mg is in extracellular compartment and the concentration is 1.5–1.9 mEq/l as normal (9, 10). The etiology of hypomagnesaemia in critical illness is complex, may involve a number of mechanisms such as decreased intake, increased renal or gastrointestinal losses, and altered intracellular or extracellular distribution (9). In the serum, Mg is divided into three fractions: ionized or active form (65%), protein bound (27%), and phosphate and bicarbonate (8%). Hypomagnesaemia mostly is asymptomatic but may present with tetany, tremor, hyperreflexia, nystagmus, ventricular arrhythmia, torsades de pointes, hypertension, coronary vasospasm, hemiparesia, bronchial airway constriction, and generalized tonic-clonic convulsions (11) such that these imbalances cause longer stay in hospitals (12). The possible mechanisms for the occurrence of Mg imbalance are the underlying disease, end organ injury, fluid and electrolyte interventions, use of medications with potential of electrolyte derangements and positive pressure ventilation (13). Previous studies have shown wide variation in prevalence of hypomagnesaemia (20-70%) in the ICU setting (14). Mg alteration is frequently observed in ICU patients, particularly in developing countries. However, these studies did not look for Mg abnormality and only one of them was conducted in a developing country (5, 15). The aim of this study was to investigate the rate of hypomagnesemia among PICU children and the related factors.

2- MATERIALS AND METHODS

2-1. Study design and population

This cross-sectional and analytical study was conducted on all one month to 12 years old children who were hospitalized in the pediatric intensive care unit (PICU) of Ali Ebne Abitalib Hospital, Zahedan University of Medical Sciences, Iran, during the year 2018. After initial stabilization, the children were monitored for serum electrolytes and clinical necessity. Children with known congenital renal magnesium wasting such as Bartter and Gitelman syndromes, patients who had

already received replacement for hypomagnesaemia in last 24 hours, patients with surgical conditions, trauma, those transferred to other PICUs, those with PICU stay less than 24 hours were excluded from the study.

2-2. Measures

Age, gender, underlying illness, electrolyte disturbances such as sodium, potassium, calcium and magnesium, duration of hospital stay and outcome were identified and recorded. Among these, admission disease category (neurological, respiratory, cardiovascular, gastrointestinal and others) were also recorded. After admission to PICU, the children were treated appropriately as per the hospital protocol. At admission, 3ml venous blood was collected in a serum vacutainer, centrifuged and serum was sent to laboratory to measure magnesium, sodium, potassium and calcium. Other routine investigations like complete hemogram, renal function test, and other relevant investigations as required for case management were performed. In the laboratory, electrolytes were measured using ion selective electrode method. The samples were analyzed for serum total calcium by the O-cresolphthalein complexone method and for serum sodium and potassium, by the ion selective electrode method. The initial diagnosis of electrolyte disturbances such as sodium and potassium, and calcium, were made as follows: hyponatremia in which sodium is lower than 135mEq/L and hypernatremia is higher than 145 mEq/L. Hypokalemia was defined when potassium is lower than 3.5 mEq/L and hyperkalemia when it was higher than 4.5 mEq/L. Hypocalcemia referred to calcium when the level was lower than 9 mg/dL and hypercalcemia when it was higher than 10.5 mg/dL. Biochemical analysis for magnesium was done using fully auto-analyzer XL 300. Magnesium level was estimated by XYLIDYL BLUE method using Erba kits. Hypomagnesaemia occurs when magnesium level is lower than 0.7 mg/dL and hypomagnesaemia when the level is higher than 2.6 mg/dL. Subjects were divided into three groups based on their serum magnesium concentration, defined hypomagnesaemia when serum magnesium was below 1.5 mg/dL, and others as normal group (16).

2-3. Ethical approval

Consent form was obtained from the participants or their guardians after the study approval. The study was approved as a GP dissertation (ethical code: ir.Zaums.rec.1394.438) by the Ethics Committee of Zahedan University of Medical Sciences, Zahedan, Iran.

2-4. Statistical analysis

Data were analyzed using SPSS 18.0 (SPSS Inc., Chicago, Illinois, USA software). Categorical data was represented in the form of frequencies and proportions. Kolmogorov-Smirnov test was used for the quantities variables to test normality distribution. Chi-square test was used as test of significance for qualitative data. Continuous data was represented as mean and standard deviation (SD). Independent t-test was the test of significance used to identify the mean difference between two groups. Logistic regression analysis was used to find the effect of different independent variables on the Mg levels at the fifth day of PICU stay. $P< 0.05$ was considered as statistically significant.

3- RESULTS

One hundred fifty children aged one month to 12 years were admitted to the PICU of Ali Ebne Abitalib Hospital, Zahedan University of Medical Sciences, during the year 2018. Of these children, 51.30% (77) were boys. The age groups distribution was 42.0%, 38.0%, 19.00% and 7.3% for <1 year, 1-5 years, 5-10 years and more than 10 years, respectively.

To perform analysis, first Kolmogorov-Smirnov test was used for the quantities variables to test normality. Normality test showed that the variables of age, weight, time of stay in PICU, magnesium, sodium, potassium and calcium had normal distribution (p>0.05). In terms of patients, height, weight and heart rate came from normal distribution (p>0.05). Children's mean weight was 11.34±9.23 Kg. The time staying in the PICU were < 6, 6-10, and >10 days with 38.7%, 18.05%, and 43.3% percentage, respectively. **Table.1** shows demographic and laboratory measures' changes based on magnesium status at PICU admission and at day 5 in PICU. From the table it was revealed that, at admitted time, age was lower in children with hypomagnesaemia (t=-2.42, p= 0.017), but the measures of weight, time spent in PICU, Na, K and Ca did not change between the two groups of children (p>0.05). All the measures were similar between hypomagnesaemia children and normal at the day 5 in PICU (p>0.05).

Table-1: The change quantities variables based on magnesium concentration levels at the admission time and after five days stay in the pediatric intensive care unit.

Variables	Magnesium Status (mg/dL)	At the time of PICU admission					At the fifth day in PICU				
		N	Mean	SD	T-value	P-value	N	Mean	SD	T-value	P-value
Age, (year)	Hypomagnesaemia	67	0.66	0.81	-2.42	0.017	51	0.73	0.92	-0.42	0.674
	Normal	83	1.01	0.96			41	0.8	0.87		
Weight, (Kg)	Hypomagnesaemia	67	9.95	8.6	-1.66	0.099	51	9.9	9.59	-0.74	0.461
	Normal	83	12.49	9.84			41	11.28	7.87		
Time staying in PICU, (Day)	Hypomagnesaemia	67	1.12	0.9	0.88	0.38	51	1.71	0.54	1.58	0.118
	Normal	83	0.99	0.92			41	1.51	0.64		
Na, (mg/dL)	Hypomagnesaemia	66	138.09	6.26	-1.1	0.272	43	137.95	7.96	-0.15	0.882
	Normal	81	139.27	6.62			33	138.21	6.79		
K, (mg/dL)	Hypomagnesaemia	66	4.39	0.62	-0.96	0.341	43	4.56	0.96	0.69	0.494
	Normal	81	4.49	0.68			33	4.42	0.65		
Ca, (mg/dL)	Hypomagnesaemia	65	8.66	0.69	-1.49	0.138	43	8.87	0.66	0.86	0.391
	Normal	81	8.83	0.63			33	8.75	0.45		

PICU: Pediatric intensive care unit, SD: Standard deviation, N: Number.

Table.2 shows the changes of the categorized variables due to the status of Mg at time of admission. 41.6% of boys and 47.90% of girls were hypomagnesaemia (p=0.432). Time staying in PICU was not associated with Mg status (p=0.618), so that, from 58 patients that stayed less than 6 days, 39.7% were in hypomagnesaemia status, from 27 patients that stayed 6-10 days, 48.1% and of 65 patients that stayed >10 days, 47.7% were hypomagnesaemia. From 101 children that took diuretic medication, 39.6%, from 130 children that took digital medication, 43.8% and from 85 children that took amino glycoside medication, 40.0% had hypomagnesaemia. Of the children admitted to the PICU, 20 of them had heart diseases with 50% hypomagnesaemia, 12 had kidney diseases with 33.3% hypomagnesaemia, 17 children had sepsis with 35.3% hypomagnesaemia, 30 children had Central nervous system (CNS) with 60.0% hypomagnesaemia and

23 had respiratory diseases with 43.5% hypomagnesaemia. From admitted children to the PICU, 58 died during stay, of which, 32(55.2%) had hypomagnesaemia (p=0.04). From the analysis it resulted that, during their stay in PICU, Na decreased (0.193), K decreased (0.901), Ca increased (0.731), and Mg decreased (0.002).

Table-2: The association between study variables and magnesium concentration at the admission time in PICU.

Variables	Groups	Statistics	Magnesium concentration at PICU admission		Total	Chi-square value	P-value
			Hypomagnesaemia	Normal			
Gender	Boys	Count	32	45	77	0.618	0.432
		%	41.6%	58.4%	100.0%		
	Girls	Count	35	38	73		
		%	47.9%	52.1%	100.0%		
Time staying in PICU	<6 days	Count	23	35	58	0.963	0.618
		%	39.7%	60.3%	100.0%		
	6-10 days	Count	13	14	27		
		%	48.1%	51.9%	100.0%		
	>10 days	Count	31	34	65		
		%	47.7%	52.3%	100.0%		
Diuretic	Yes	Count	40	61	101	3.206	0.073
		%	39.6%	60.4%	100.0%		
	No	Count	27	22	49		
		%	55.1%	44.9%	100.0%		
Digitals	Yes	Count	57	73	130	0.26	0.606
		%	43.8%	56.2%	100.0%		
	No	Count	10	10	20		
		%	50.0%	50.0%	100.0%		
Aminoglycoside	Yes	Count	34	51	85	1.728	0.189
		%	40.0%	60.0%	100.0%		
	No	Count	33	32	65		
		%	50.8%	49.2%	100.0%		
Outcome	Dead	Count	32	26	58	4.223	0.04
		%	55.2%	44.8%	100.0%		
	Alive	Count	35	57	92		
		%	38.0%	62.0%	100.0%		
Heart Diseases	Yes	Count	10	10	20	0.266	0.606
		%	50.0%	50.0%	100.0%		
	No	Count	57	73	130		
		%	43.8%	56.2%	100.0%		
Kidney Diseases	Yes	Count	4	8	12	0.678	0.41
		%	33.3%	66.7%	100.0%		
	No	Count	63	75	138		
		%	45.7%	54.3%	100.0%		

Sepsis	Yes	Count	6	11	17	0.681	0.409
		%	35.3%	64.7%	100.0%		
	No	Count	61	72	133		
		%	45.9%	54.1%	100.0%		
Central nervous system (CNS)	Yes	Count	18	12	30	3.567	0.059
		%	60.0%	40.0%	100.0%		
	No	Count	49	71	120		
		%	40.8%	59.2%	100.0%		
Respiratory Diseases	Yes	Count	10	13	23	0.016	0.901
		%	43.5%	56.5%	100.0%		
	No	Count	57	70	127		
		%	44.9%	55.1%	100.0%		
Other Diseases	Yes	Count	19	29	48	0.738	0.39
		%	39.6%	60.4%	100.0%		
	No	Count	48	54	102		
		%	47.1%	52.9%	100.0%		
Total		Count	67	83	150		
		%	44.7%	55.3%	100.0%		

PICU: Pediatric intensive care unit**.**

Table.3 shows the results of logistic regression to find the predicted factors for hypomagnesaemia at the day fifth after admission. As the 95% confidence interval (CI) overlapped, compared to those aged <1 year as a reference group, 1-5-year-old children had 1.37 times higher odds (95% CI=10.54 to 3.46), and >5-year-old children had 1.79 times higher odds (95% CI=0.76 to 8.30) to be hypomagnesaemia. Same trends were observed for sex so that compared to boys, girls had 1.01 times higher odds (95% CI=0.44 to 2.30) to be hypomagnesaemia. Children with diuretic prescription had 2.24 times higher odds (95% CI=0.93 to 5.42) to be hypomagnesaemia compared to those children that were not prescribed a diuretic. Same trends were observed for the digital and aminoglycoside, in children that were hypokalemia, hyponatremia and hypocalcemia the odds of hypomagnesaemia were 0.51 (95% CI=0.08 to 3.23), 1.01(95% CI=0.35 to 2.94), and 1.04 (95% CI=0.34 to 3.19). Length of hospitalization was considered as <= 10 days and >10 days' groups. To compare with <=10 days, those who stay more in the PICU had 1.69 (95% CI= 0.69 to 4.13) times higher odds. Those children were that admitted to the PICU due to heart disease compared to those who did not have heart diseases, had 0.17 (95% CI=0.04 to 0.66) times higher odds to be hypomagnesaemia, that showed a significant effect because the confidence interval bounds did not overlap. Other diseases in children admitted to the PICU had the same trends but no significant effects were observed.

Table-3: Odds of predictor variables on the levels of magnesium concentration.

Variables	Normal magnesium N (%)	Hypomagnesemia N (%)	P-value	Odds Ratio (95 % CI)
Age (year)				
<1	23 (51.1)	22 (48.9)	Ref.	1
1-5	13 (43.3)	17 (56.7)	0.509	1.37 (0.54, 3.46)
>5	5 (29.4)	12 (70.6)	0.132	2.51 (0.76, 8.30)
Gender				
Male	21 (44.7)	26 (55.3)	Ref.	1
Female	20 (44.4)	25 (55.6)	0.98	1.01 (0.44, 2.30)
Diuretic				
No	30 (51.7)	28 (48.3)	Ref.	1
Yes	11 (32.4)	23 (67.6)	0.074	2.24 (0.93, 5.42)
Digitals				
No	35 (44.3)	44 (55.7)	Ref.	1
Yes	6 (46.2)	7 (53.8)	0.9	0.93 (0.29, 3.01)
Amino				
No	25 (54.3)	21 (45.7)	Ref.	1
Yes	16 (34.8)	30 (65.2)	0.061	2.23 (0.96, 5.17)
Hyponatremia (Na<135)				
No	25 (44.6)	31 (55.4)	Ref.	1
Yes	8 (44.4)	10 (55.6)	0.988	1.01 (0.35, 2.94)
Hypokalemia (K<3.5)				
No	30 (43.5)	39 (56.5)	Ref.	1
Yes	3 (60.0)	2 (40.0)	0.513	0.51 (0.08, 3.23)
Hypocalcemia (Ca<8.5)				
No	26 (44.8)	32 (55.2)	Ref.	1
Yes	7 (43.8)	9 (56.3)	0.939	1.04 (0.34, 3.19)
Length of hospitalization (day)				
<=10	15 (53.6)	13 (46.4)	Ref.	1
>10	26 (40.6)	38 (59.4)	0.252	1.69 (0.69, 4.13)
Heart diseases				
No	30 (38.5)	48 (61.5)	Ref.	1
Yes	11 (78.6)	3 (21.4)	0.011	0.17 (0.04, 0.66)
Kidney diseases				
No	39 (45.9)	46 (54.1)	Ref.	1
Yes	2 (28.6)	5 (71.4)	0.385	2.12 (0.39, 11.54)
Sepsis				
No	36 (44.4)	45 (55.6)	Ref.	1
Yes	5 (45.5)	6 (54.5)	0.95	0.96 (0.27, 3.40)
Central nervous system diseases				
No	31 (47.0)	35 (53.0)	Ref.	1
Yes	10 (38.5)	16 (61.5)	0.461	1.42 (0.56, 3.58)
Respiratory diseases				
No	39 (47.0)	44 (53.0)	Ref.	1
Yes	2 (22.2)	7 (77.8)	0.173	3.10 (0.61, 15.83)

95% CI: 95% Confidence Interval.

4- DISCUSSION

The present study aimed to evaluate the prevalence of hypomagnesaemia in children admitted to the pediatric intensive care unit (PICU) and its related factors in Zahedan. From the study, it was resulted that 44.7% of the patients had hypomagnesaemia. These patients had lower age weight, longer hospital stay, higher levels of Na, K and Ca, but not significant. During the first five days staying in PICU, 58 children died, most of whom were hypomagnesemia. Mg levels ranged from approximately 11 to 60% in PICU admissions in different studies (17-20). Soliman et al. (17) reported 18%, and Haque and Saleem (18) reported 44.1%, mostly older than 1 year of age. Limaye et al. (19) reported 52%, which is close to the results of the present study (44.6%).

Gholyaf et al. (21) conducted a study on patients admitted to ICU. They concluded that Mg did not have a relationship with age and gender. Soliman et al. (17) concluded that hypomagnesemia patients had longer duration of ICU stay, and a greater mortality rate. In the same line, Haque and Saleem (18) found sepsis, hypokalemia, hypocalcemia, diuretic, aminoglycoside use, and hospital stay more than five days were the most important risk factors for hypomagnesemia. As compared to patients with normal Mg, Limaye et al. (19) also reported that, those with hypomagnesemia had a longer duration of PICU stay. It has been shown that the serum Mg level was markedly reduced among patients with sepsis due to acute bacterial infection (19, 22, 23). Erdogan and Menevse (23) observed that the majority of their ICU patients had respiratory diseases (30.69%), neurological diseases (25.74%), and sepsis (19.80%). They also found, the patients with hypomagnesemia had a greater mean age and longer ICU stay, having nasogastric drainage, and higher mortality rate. Gupta et al. (24) showed that administering hypocalcemia and hypokalemia were not sufficient to correct hypocalcemia and hypokalemia in PICU, and stressed that hypomagnesemia and serum magnesium level should be corrected. They also revealed that the levels of rates of hypokalemia, hypocalcemia, hypophosphatemia, and hypoalbuminemia were significantly higher in hypomagnesemia patients. A greater incidence of electrolyte abnormalities and a strong association of hypomagnesemia with sepsis and septic shock can explain the higher mortality rates in the hypomagnesemia patients. The frequency of calcium, magnesium and phosphorus deficiency in the given orders is high at admission and calcium and magnesium deficiency frequency changed gradually 3 to 10 days after admission, while phosphorus level declined. Respiratory is not an organ that was a reason for failure in children and then neurological. Children with hypocalcaemia had a higher hypomagnesaemia, and those who were admitted due to sepsis diagnosis had hypomagnesaemia status (23-26).

Safavi and Honarmand (26) reported that hypocalcemia, hypokalemia, and hyponatremia were more common among hypomagnesemia in PICU especially for those who were older than 16 years of age. They also found that at admission, 51% of patients had hypomagnesemia. A significant difference was found in the hospital or ICU stay regarding Mg levels. Hypomagnesemia patients more frequently had total hypocalcemia, hypokalemia, and hyponatremia. 51 patients developed hypomagnesemia during their ICU stay. Previous studies reported that hypomagnesemia was more prevalent among patients using diuretics and aminoglycosides (27), similar to the present study. Diuretics effect by inhibiting magnesium absorption. Aminoglycosides cause urinary

magnesium excretion by impairing magnesium reabsorption in loop and distal tubules. As the number of our patients using aminoglycosides was so low, we excluded them; we did not detect any difference with regard to diuretic use, either. Magnesium plays an important role for immunological functions such as macrophage activation, adherence, lymphocyte proliferation, endotoxin binding to monocytes (28). It has been found that potassium and other electrolytes abnormalities are the main causes of hypomagnesemia. This proves a correlation between electrolyte abnormalities in critically ill children that affected the level of Mg (12.29). Using different medications in PICU is common and may contribute to the electrolyte disturbances as they can interfere with the absorption of electrolytes, alter hormonal responses affecting hemostasis and can directly affect the organ function. Their requirement, however, indicates the severity of illness and they continue to be an important risk factor for later development of electrolyte imbalance (2).

Hypomagnesemia is known to cause muscle weakness and respiratory failure and difficulty in weaning the patient from the ventilator as well. A greater incidence of electrolyte abnormalities and a strong association of hypomagnesemia with sepsis and septic shock similar and comparable with the present study results (24) can explain the higher mortality rates in the hypomagnesemia patients. This is due to the fact that the renal potassium loss is increased in the presence of hypomagnesemia such that hypocalcemia is a well-known manifestation of Mg deficiency especially in youngers (26); they stressed the combination of hypokalemia and hypomagnesemia may have originated from underlying conditions that may have affected the levels of this electrolytes (18). Singhi et al. (9) resulted that Mg deficiency as often as possible creates a wide assortment of clinical conditions, for example, protein–vitality ailing health malabsorption, hypoalbuminemia, sepsis, hypothermia, and so on, conditions that are regularly found in youngsters in developing nations. Some possible explanations for lack of correlation between Mg and clinical outcome in different studies could be the heterogeneous patient population in every study and the fact that serum Mg measurement is not a reliable indicator of the real magnesium status of the body.

4-1. Study Limitations

There were several limitations in the present study. First, it was a single center study; and may not represent the findings at other centers in Sistan and Baluchistan province, Iran. Second, being a retrospective study, it was not possible to assess all the variables and the author had limited scope of the completeness of documentation by the treating physician. Finally, follow up magnesium levels were not done. Total serum magnesium level was measured instead of ionized magnesium.

5- CONCLUSION

From the study, it was concluded that that the prevalence of hypomagnesaemia in children admitted to the pediatric intensive care unit is high and it is often associated with hypokalemia, hypocalcaemia, hypoalbuminemia. Hypomagnesaemia causes higher mortality and longer hospital stay. It is recommended that magnesium concentration levels should be included routinely in the electrolyte panel for monitoring critically ill patients.

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7- CONFLICT OF INTEREST: None.

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