Causes and outcome of abnormal liver functions during pregnancy: a cross-sectional study

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Background and aim
Liver diseases during pregnancy, whether related or not to pregnancy, represent a challenge in their diagnosis and management. The aim of this study was to investigate the frequency of different liver diseases that affect pregnant women in our locality and their impact on the outcomes of pregnancy. It also aims to study the effect of pregnancy termination on the patients' laboratory parameters.
Patients and methods
In total, 344 pregnant women with abnormal liver functions were included in this study. All study participants underwent the routine clinical and laboratory evaluation to diagnose the cause of their hepatic dysfunction. They were followed up until 1 week after delivery to record the maternal and fetal outcomes.
Results
The most common diseases related to pregnancy were the hypertensive disorders (43.9%). Chronic viral hepatitis was the most common disease not related to pregnancy (38.9%). Most cases (69.1 and 44.1%) had good maternal as well as fetal outcome successively. The frequencies of maternal mortality and fetal loss were 4.1 and 17.1% successively.
Conclusion
Pregnancy-related hypertensive disorders and chronic viral hepatitis were the most common causes of liver diseases among pregnant women. Most cases showed favorable fetal and maternal outcome.

Keywords:
abnormal liver profile, hepatic affection in pregnancy, liver disease in pregnancy, viral hepatitis in pregnancy

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Introduction

Liver disease is a serious condition during pregnancy that represents a challenge for both gynecologists and hepatologists. It occurs in ~3% of all pregnancies, with mortality rate of 0–25% among mothers [1,2].

They are classified into disorders related to pregnancy, such as hyperemesis gravidarum, pregnancy-induced hypertensive disorders, acute fatty liver of pregnancy, and intrahepatic cholestasis of pregnancy and disorders not related to pregnancy, such as acute and chronic viral hepatitis, autoimmune hepatitis, drug-induced hepatitis, alcoholic and nonalcoholic steatohepatitis, and intrahepatic and extrahepatic biliary diseases with or without cirrhosis [3,4].

Aim

This study aims to investigate the frequency of different liver diseases affecting pregnant women and the effect of pregnancy termination on the course of liver disease. The study also aims to explore the impact of liver diseases during pregnancy on maternal and fetal outcomes.

Patients and methods

The study was conducted in Zagazig University Maternity Hospital and Tropical Medicine Department. The details of the study and terms of participation were explained to all participants. All patients accepted to participate in the study and know that the participation is voluntary and that they can withdraw from the study whenever they want to. They also know that the resources of the study are provided by Zagazig university hospitals. The study included 344 pregnant women with abnormal liver-function tests. Patients who refused to participate in the study and patients who delivered their babies outside the Zagazig University Maternity Hospital were excluded from the study. The study design was revised and approved by the IRB of Faculty of Medicine, Zagazig University.

All patients were subjected to the following: full history taking, thorough clinical examination, routine

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laboratory investigations; liver-function and kidney-function tests, complete blood count, coagulation profile, 24-h urinary protein, viral markers HCV Ab and HBsAg, and autoimmune markers antinuclear antibody and anti-smooth muscle antibody, anti-liver kidney microsomal antibody whenever autoimmune hepatitis is suspected. Obstetric ultrasound was performed to all patients to confirm viability, gestational age, fetal presentation, amount of liquor, detailed assessment of placental site, and fetal well-being. Patients also performed abdominal ultrasound examination with focus on the manifestations of hepatic affection, liver size and echogenicity, spleen size, gall bladder disease, and ascites.

Follow-up of all patients was performed during pregnancy while receiving the conventional treatment unique for their condition, till termination of pregnancy and re-evaluation of their condition was done 1 week after termination.

Assessment of maternal outcome included the following: maternal mortality, hemorrhage, sepsis, liver failure, ICU admission, and need for blood transfusion. Assessment of fetal outcome was also performed to detect intrauterine fetal death/abortion, as well as intrauterine fetal growth retardation and neonates were examined after birth for signs of distress and need for neonatal ICU admission and APGAR scoring.

Statistical analysis

Analysis of data was done using SPSS Epi Info, version 16 (CDC, Atlanta, Georgia, USA). Categorical data were represented as number and percentage and compared using χ^2 test. Continuous data were represented as mean and SD for normally distributed data and median and range for data that lack normal distribution criteria. Normally distributed data were compared using t test, otherwise, with data with no normal distribution, Mann–Whitney test was used to compare data ranks.

Results

The study included 344 pregnant women with evidence of hepatic affection during pregnancy. Table 1 represents a summary of the demographic data of the studied population. It shows that the majority of women were between 26 and 35 (52.3%) with a mean age of 34 years. It also shows that most females were G2 (65.9%).

Figure 1 represents the most common presenting symptoms of liver disease among pregnant women in the study. It shows that in the highest percentage of conditions, women were diagnosed during the antenatal follow-up schedule without any presenting symptom (22.3%). It also shows that the most common presenting symptoms were lower-limb edema and jaundice in 18% of cases and vomiting in 17% of cases followed by bleeding tendency in 11.6% of cases. Abdominal pain and pruritis were the least common symptoms with frequencies of 6.9 and 4.6% successively.

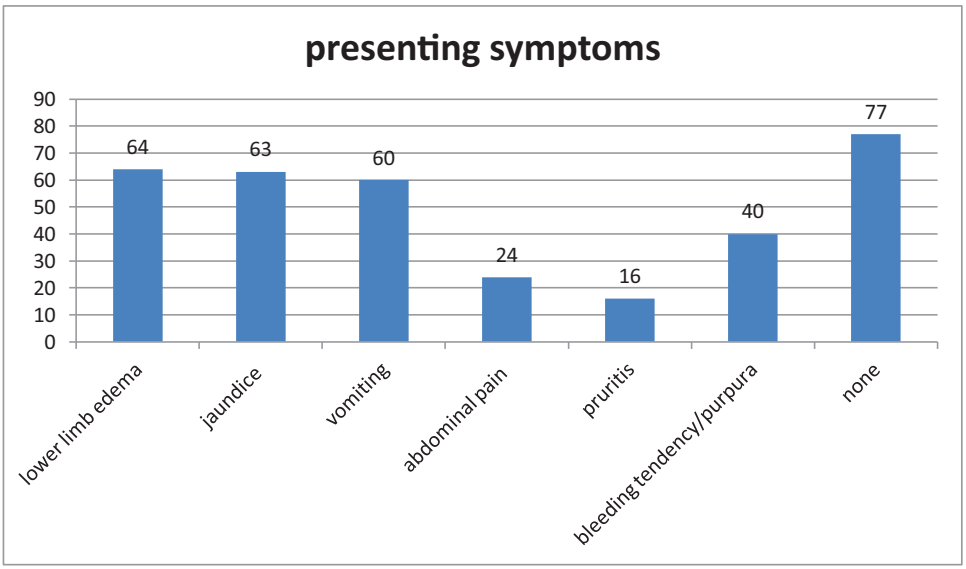
Table 1 Demographic data of the studied population

	N=344 [*n* (%)]
Age (years)	
<25	99 (28.77)
26–35	180 (52.32)
36–45	65 (18.8)
Mean±SD	34.4±10.6
Gravidity	
G1	83 (24.1)
G2	226 (65.9)
G3	24 (6.9)
G4	11 (3.1)
Residence	
Urban	255 (74.1)
Rural	89 (25.9)
Comorbidities	
Hypertension	34 (9.8)
Diabetes	29 (8.4)
Cardiac	13 (3.8)

The overall frequency of pregnancy-related liver diseases was 53.8%, while the frequency of liver disease not related to pregnancy was 46.2%. Figure 2 represents the frequency of the different liver diseases related to pregnancy among the studied population. It shows that liver diseases related to pregnancy represented 53.8% of the total studied population. The most common causes of hepatic dysfunction related to pregnancy were hypertensive disorders of pregnancy (43.9%), preeclampsia (25%), HELLP syndrome (12.5%), and antepartum eclampsia (6.4%) followed by hyperemesis gravidarum with frequency of 4.6%. The least common liver diseases related to pregnancy among the studied population were acute fatty liver of pregnancy and intrahepatic cholestasis of pregnancy with frequencies of 2.9 and 2.3% successively.

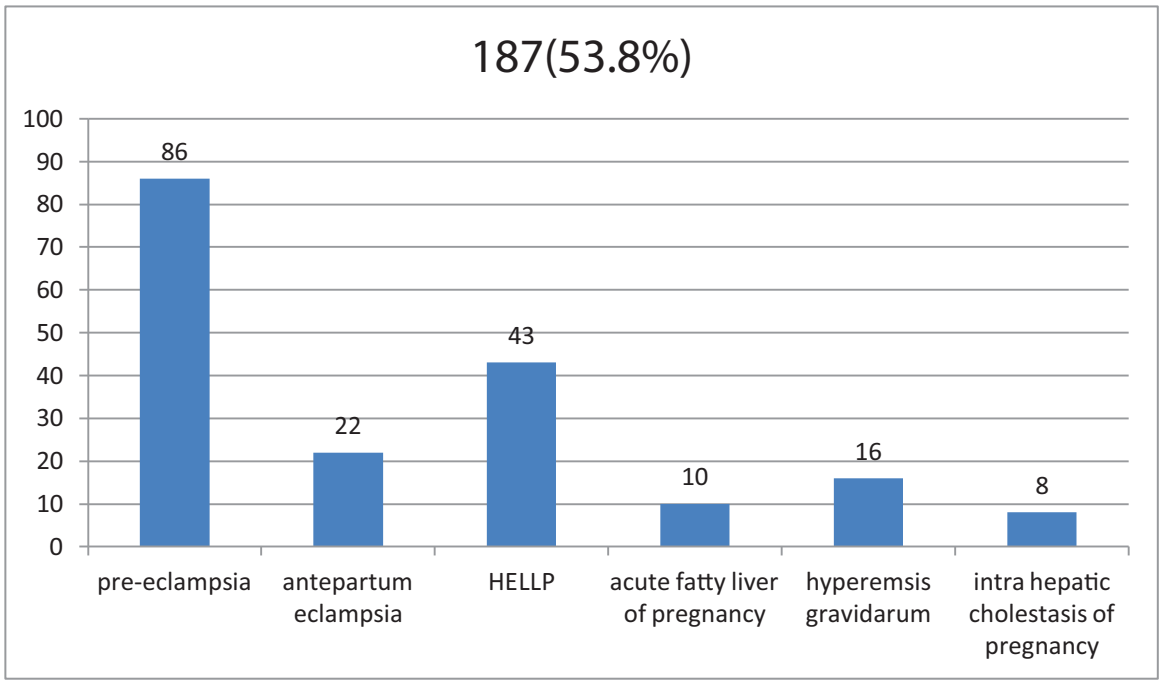
Figure 3 represents the different liver diseases not related to pregnancy among the studied population. It shows that they represent 46.2% of the overall studied population. Chronic viral hepatitis comes on the top of the list with frequency of 38.9%, 27.3% for HCV, and 11.6% for HBV. Autoimmune hepatitis was also found in 1.6% of the studied participants. Calcular cholecystitis was found in 2.3% of cases. Cirrhosis was

Figure 1



Frequency of different presenting symptoms of liver disease among the studied population.

Figure 2



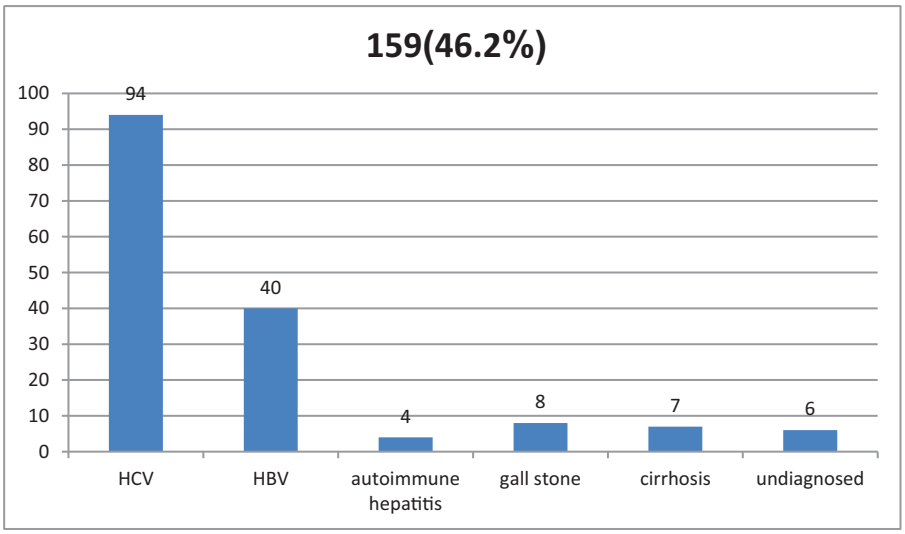
Frequency of different liver diseases related to pregnancy among the studied population.

found in 2% of cases, while in 1.7%, the final diagnosis of liver disease was not reached.

Table 2 represents the most common clinical and sonographic signs of liver disease detected among the studied population. It shows that in the majority of conditions, the liver was normal in size (82.5%). Liver was enlarged in 15.4% of cases and spleen was also enlarged in 4.1%. Ascites were detected in 18.3% of cases. Table 3 represents a comparison of the patients' laboratory parameters before and 1 week after termination of pregnancy. It shows that there is a highly significant improvement noted in almost all patients' parameters, except hemoglobin, which showed no significant difference.

Figure 4 represents the frequency of different maternal outcomes of liver disease during pregnancy. It shows that with the standard of care specific for each disease, 69.1% pass uncomplicated. It also shows that 4.3%

Figure 3



Frequency of liver diseases not related to pregnancy among studied population.

Table 2 Clinical and sonographic data of the studied population

	N=344 [*n* (%)]
Splenomegaly	14 (4.1)
Liver	
Enlarged	53 (15.4)
Shrunken	7 (2.1)
Normal	284 (82.5)
Ascites	63 (18.3)

Table 3 Comparison of laboratory data of the studied population before and 1 week after termination

	Before (*N*=344)	After (*N*=330)	Test	*P* (significance)
Hemoglobin concentration (g/dl)				
Mean±SD	9.6±3.8	9.9±3.5	t=1.06	0.28 (NS)
Platelet count (×10^9 cell/μl)				
Mean±SD	107.7±33.4	167±29.6	t=24.3	<0.001 (HS)
INR	1.4±0.2	0.9±0.2	t=32.4	<0.001 (HS)
Creatinine (mg/dl)	1.3±0.3	0.7±0.3	t=25.9	<0.001 (HS)
Proteinuria [*n* (%)]	158 (45.9)	10 (2.9)	χ^2=165	<0.001 (HS)
Albumin (g/dl)	2.6±1.2	3.1±1.4	t=4.6	<0.001 (HS)
Bilirubin (mg/dl)	2.1±0.2	1.2±0.2	t=58.4	<0.001 (HS)
ALT (IU/L)				
Median	194	55		<0.001 (HS)
Range	29–333	16–170		
AST (IU/L)				
Median	155	55		<0.001 (HS)
Range	40–330	12–150		

ALT, alanine aminotransferase; AST, aspartate aminotransferase; HS, highly significant; INR, international normalized ratio; NS, nonsignificant.

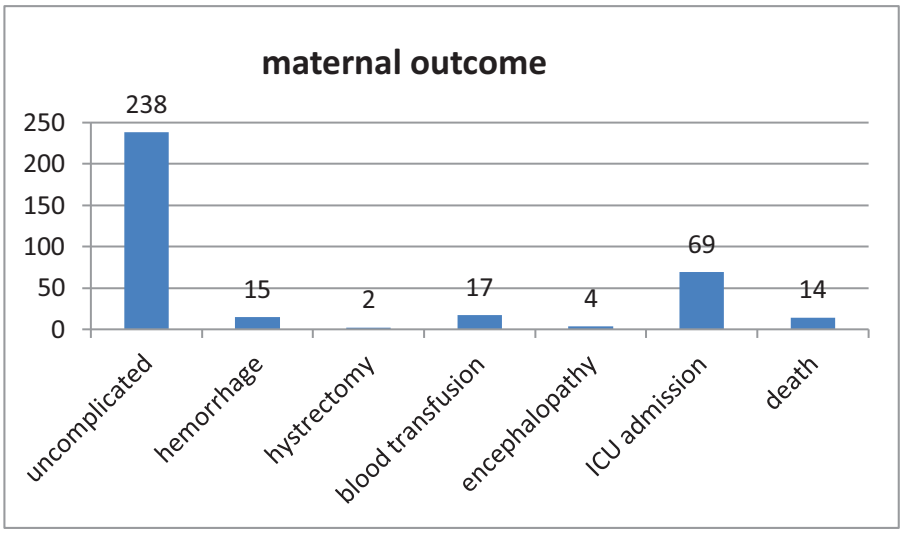
experienced hemorrhage, 4.9% needed blood transfusion, and 0.5% needed hysterectomy due to severe uncontrollable postpartum hemorrhage. It also shows that 20% needed ICU admission and hepatic encephalopathy was seen in 1.2 and 4.1% died. The disease that was related to the severe complication and ICU admission and mortality was acute fatty liver of pregnancy followed by complicated cases of preeclampsia. Acute fatty liver of pregnancy was associated with hepatic encephalopathy and coagulopathy and severe bleeding. The third cause of severe complications and mortality was HELLP syndrome.

Figure 5 represents the different fetal outcomes. It shows that 44.1% of babies were delivered at full term in good health and needed no further intervention, while 18% were delivered before full term and that 20% of babies needed neonatal ICU admission. Abortion and IUFD were seen in 12.2 and 4.9% of cases successively.

Discussion

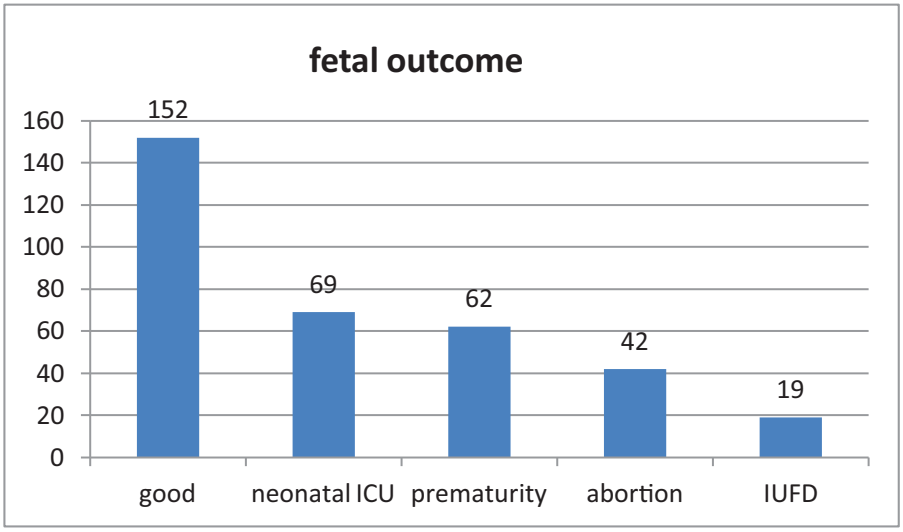
Liver diseases during pregnancy represent a challenge to both gynecologists and heptologists. The condition is more or less a double jeopardy because of the impact of pregnancy on the course of liver disease and the impact of liver disease on the outcomes of pregnancy. This study aims to identify the most common liver diseases that affect pregnant women in our locality, the most common presenting symptoms that should draw the healthcare providers' attention to hepatic affection, as well as the impact of termination on liver condition. It also aims to study the impact of this hepatic affection on the fetal and maternal outcomes.

Figure 4



Frequency of liver diseases not related to pregnancy among the studied population.

Figure 5



Fetal outcome of liver disease.

In this study, we found that more than 50% of patients were aged 26–35 years old. It is also worth noticing that more than 65% were presented in their second pregnancy. The correlation between liver disease and second pregnancy or any specific age group is not mentioned in any of the previous literature, hence it is considered a topic for further research.

About the presenting symptoms, it is worth to mention that the highest percentage of our study participants was discovered during the antenatal care follow-up schedule without any specific presenting symptom. This may be attributed to the finding that chronic viral hepatitis was the most common liver disease among pregnant women in our study, a condition that is asymptomatic in most cases.

Another explanation of this is that lower-limb edema and vomiting, which are found to be the most common presenting symptoms among pregnant women in our study, were perceived by most women as normal symptoms of pregnancy. This should draw the attention of healthcare providers to educate women that lower-limb edema especially early in pregnancy

can be a sign of hypertensive disorders of pregnancy and that intractable vomiting can also refer to hyperemesis gravidarum.

This finding refers to the importance of the antenatal care and follow-up schedule, and to the importance of screening pregnant women for the presence of HCV and HBV markers in their serum. This agrees with García-Romero *et al.* [5], who said that liver diseases during pregnancy may have an inconspicuous clinical presentation [5].

Lower-limb edema was the most frequent symptom of hepatic affection among pregnant women in our study. This can be attributed to the finding that hypertensive disorders of pregnancy (preeclampsia, eclampsia, and HELLP syndrome) were the most common cause of pregnancy-related hepatic affection in pregnant women in our study (43.9%) and edema is a cardinal symptom for this category of disorders. This agrees with Ch'ng *et al.* [6] and Rathi *et al.* [7], who said that preeclampsia is the cause of nearly 50% of conditions of hepatic affection among pregnant women. It was followed by vomiting and jaundice and then bleeding tendency [6,7]. This also agrees with Kingham [8], who said that pregnancy-induced hypertensive disorders are the most common cause of hepatic dysfunction during pregnancy [8]. Pruritis was the least common presenting symptom and this may be attributed to the finding that the cholestatic diseases were the least common among pregnant women in our study. This agrees with Ahmed *et al.* [3], who said that intrahepatic cholestasis of pregnancy has a low prevalence among pregnant women (0.5–1%) [3].

This also agrees with García-Romero *et al.* [5], who said that the incidence of intrahepatic cholestasis of pregnancy differs from country to country and in different ethnic groups and it is rarely found in African countries.

Our study shows that the diseases related to pregnancy were rather more frequent than those not related to pregnancy (53.8 vs. 46.2%). This agrees with Kingham [8] and Wong *et al.* [9]; however, the pregnancy-related diseases in Wong *et al.* [9], study were much more frequent (85%). This may be due to the fact that the prevalence of chronic viral hepatitis in our locality is higher than recorded worldwide [8].

It is also worth noticing that ascites were evident in 18% of patients, while cirrhosis was seen only in 2% of them. This indicates that in most instances, ascites were rather related to proteinuria and renal dysfunction associated with pregnancy-induced hypertensive disorders than to hepatic decompensation. Moreover, patients with acute fatty liver of pregnancy who represent 5% of patients with liver disease often present with minimal ascites.

The comparison of patients' laboratory parameters before and 1 week after termination of pregnancy revealed a significant improvement of liver and kidney functions, as well as coagulation profile and platelet count, with no significant effect on the hemoglobin concentration. This improvement was also associated with symptom relief as well as decline of blood pressure and edema. We also noted that most ascetic patients showed an improved response to diuretic therapy than during pregnancy and almost all of them experienced disappearance of ascites.

Most cases in our study had favorable outcome, this may be because the most common cause of liver disease among pregnant women with liver disease in our study was chronic viral hepatitis and it is well known that chronic viral hepatitis, if it is not complicated with cirrhosis and liver cell failure, does not have an impact on the outcome of pregnancy [9].

Acute fatty liver of pregnancy appears to be responsible for the worst maternal and perinatal outcome. In our study, most cases of hepatic encephalopathy were related to acute fatty liver of pregnancy. This comes in agreement with what was found by Rathi *et al.* [7], who reported that patients with acute fatty liver of pregnancy suffered from nausea, vomiting, and upper-abdominal pain preceding jaundice complicated by encephalopathy, renal failure and coagulopathy, intractable bleeding, and death [7].

In the highest percentage of cases, the fetal outcome was good. This is attributed to the finding that chronic viral hepatitis, being the most common condition, has a very low impact on the fetus. Since termination was found to be the ultimate cure in most cases, the most common fetal unfavorable outcome was prematurity. This was also the most important cause of neonatal ICU admission.

Conclusion

The most common cause of liver affection among pregnant women in our locality was chronic viral hepatitis followed by pregnancy-induced hypertensive disorders. The conditions that were associated with the worst prognosis were acute fatty liver of pregnancy, complicated preeclampsia, and HELLP. Most cases were discovered accidentally

during the routine antenatal follow-up. Termination of pregnancy leads to a remarkable improvement of the patients' condition. With good antenatal care, most cases have favorable maternal and fetal outcome.

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Conflicts of interest

There are no conflicts of interest.

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