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Preeclampsia symptoms and liver function tests in women with pre-eclampsia: comparison with a normal pregnant woman

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A B S T R A C T

Preeclampsia is a pregnancy-related condition that is linked to elevated blood pressure and proteinuria. It is one of the main causes of child and mother deaths in developed countries and only affects pregnant women during the second and third trimesters of pregnancy. Due to normal hepatic markers during pregnancy, the purpose of this study is to examine these factors in pregnant women and their association with disorders such as preeclampsia. Thus, the liver function tests in pre-eclampsia and normal pregnancy were compared. This study included 100 pregnant women after 20 weeks of pregnancy, divided into two groups, Group A is the preeclampsia group, which consisted of 60 preeclamptic women, whose blood pressure was greater than 140/90 mm Hg and whose proteinuria in a 24-hour period was greater than 300 mg. and Group B is the control group, which consisted of 40 pregnant women with normal blood pressure, The Obstetrics and Gynecology Department of the Teaching Governmental Hospital in the northeastern Libyan city of El-Baida provided the samples. In both groups, study assessed the serum activities of the liver enzymes ALT, and AST, and the level of total bilirubin. According to the findings, there was no discernible difference between the two groups' total bilirubin levels. The serum activities of ALT and AST across the two groups did, however, differ significantly ($p<0.05$). The results of this study indicate that preeclampsia-affected pregnant women had hepatic biomarkers that were higher than those of healthy pregnant women.

1 Introduction

In around 5%–10% of all pregnancies, hypertension during pregnancy raises the risk of complications (Cunningham *et al.*, 2010). It is third only to hemorrhage and embolism in terms of the primary causes of pregnancy-related mortality, and it causes severe maternal and perinatal morbidity (Mackay *et al.*, 2001 and Munazza *et al.*, 2011). According to Jeyabalan, 2013 and Panda & Mondal, 2018 preeclampsia (PE) is a syndrome that only affects pregnant women during the second and third trimesters of pregnancy and can impact different organ systems. It rarely occurs before 20 weeks of pregnancy, like in hydatidiform moles (Dutta, 1998 and Patil *et al.*, 2016).

Vasoconstriction and thickening of the vascular medium, that reduce vascular capacity and raise peripheral resistance, are the primary causes of preeclampsia (Munazza *et al.* 2011). Preeclampsia's exact aetiology is still not well understood. (Munazza *et al.*, 2011). Almost every organ is impacted. placenta, maternal immune response, vascular illness, genetic predisposition, and low calcium levels in the mother are some of the variables that seem to play a part. Preeclampsia has a placental origin, and placenta removal at birth is the first step in preeclampsia treatment. (Cnossen *et al.*, 2006 and Munazza *et al.*, 2011). The increase in peripheral vascular resistance in these ladies is probably what is causing their hypertension.

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PE 3 million preterm birth has unclear underlying pathophysiology, but it is currently thought that reduced placental perfusion—which results from shallow cytotrophoblast migration toward the uterine spiral arterioles and causes inappropriate vascular remodeling and a hypoperfused placenta is the primary initiating event in PE (Roberts & Gammill, 2005 and Amaral *et al*., 2015). As the pregnancy progresses, this placenta becomes ischemic, which causes the release of substances that promote maternal vascular endothelial dysfunction (Amaral *et al.*, 2015). One of the main phenotypes of preeclampsia, endothelial dysfunction causes broad vasoconstriction and decreased blood flow to numerous organs. Additionally, pre-existing illnesses like inadequate nutrition, diabetes, and obesity are risk factors for PE and may worsen the mother's reaction to substances released from an ischemic placenta (Brennan *et al.*, 2014).

While 800 women die from pregnancy complications around the world every day, 3 million preterm births reported each year are related to preeclampsia (Serrano *et al.*,2004, Kinney *et al*., 2012, and Amaral *et al.*, 2015). Other than an early birth of the fetus, there is no effective treatment for this pregnancy illness (Amaral *et al.*, 2015).

According to the working group categorization, PE is identified when a pregnant woman presents with proteinuria (i.e., urinary protein ≥300 mg/24 h or ≥1+ dipstick). and high blood pressure (BP), which is defined as BP ≥140/90 mm Hg. (Moser, 2001, Mammaro *et al*., 2009, Cunningham *et al.*, 2010, and Panda & Mondal, 2018). High blood pressure is linked to considerable organic dysfunction after 20 weeks of pregnancy, as well as a high maternal mortality rate due to complications like eclampsia, HELLP syndrome, and edema (Kedziora *et al*., 2021). Severe preeclampsia is defined by one or more of the following criteria: elevated blood pressure 160 mmHg systolic, or 110 mmHg diastolic, on two occasions at least 6 hours apart, on bed rest; with proteinuria ≥5 g in a 24-hour urine collection; and it is characterized by at least one of the following functional symptoms: headache, hyperreflexia, oliguria, epigastric or right upper quadrant pain, impaired liver function, and thrombocytopenia (HELLP syndrome). (Munazza *et al*., 2011).

Preeclampsia is further complicated by the involvement of the liver and kidney to varying degrees (Townsend *et al.*,2016 and Panda & Mondal, 2018). Liver involvement manifested as right upper quadrant abdominal pain or elevated transaminase levels, is one of the main clinical features of preeclampsia (Nachshon *et al.*, 2022). The liver is a vital organ in our bodies that performs numerous functions. The levels of serum alanine aminotransferase (ALT) and aspartate aminotransferase (AST) are normal. As a result, measuring these enzymes during pregnancy can be used to diagnose liver disease (Bacq, 2000-2013 and Panda & Mondal, 2018). Preeclampsia is the most common cause of liver function test (LFT) abnormalities, which occur in 3% of pregnancies (Angel, 2000, Munazza *et al*., 2011, and Das *et al*., 2013). The liver diseases peculiar to pregnancy have a characteristic time of onset. In the last trimester, liver disease with abnormal LFT, nausea and/or vomiting, and abdominal pain is caused by severe preeclampsia, HELLP syndrome, or acute fatty liver of pregnancy with or without sub-capsular hepatic haematomas, which overlap (Burroughs, 1998, and Munazza *et al*., 2011). Patients with HELLP syndrome are subsets of those with severe preeclampsia who are more likely to experience multiple system dysfunction (Weinstein,1982, Munazza *et al*., 2011, and Das *et al*., 2013). During Pre-eclampsia liver dysfunction has serious consequences. An increase in LFT results is observed in pre-eclampsia with HELLP syndrome.

ALT and AST levels may be elevated as well, and hyperbilirubinemia may occur, particularly in the presence of haemolysis. The lesion that causes elevated serum liver enzyme levels is most likely periportal hemorrhagic necrosis in the periphery of the liver lobule. Haemorrhage under the liver capsule can be so severe that the capsule ruptures, resulting in potentially fatal intraperitoneal bleeding (Simith *et al*., 1991, Burroughs, 1998, Munazza *et al.*, 2011, Das *et al*., 2013, and Lodhi & Roy, 2018). Analyses of hepatic function and integrity, such as AST, ALT, lactate dehydrogenase (LDH), bilirubin, albumin, and international normalized prothrombin time ratio, are frequently quantified in the routine clinical management of women with PE. Previous research has yielded conflicting results regarding the ability of LFT to predict adverse maternal outcomes. While some studies found strong associations between AST, ALT, LDH, and bilirubin levels and adverse outcomes, others found only weak or no associations (Magann *et al*., 1993, Sibai, 2004, Dadelszen *et al.*, 2004, Hupuczi *et al*., 2007, and Kozic *et al*., 2011). LDH reflects both hemolytic cell damage and hepatic dysfunction, bilirubin reflects both hemolysis and hepatic dysfunction, and AST reflects both tissue damage and hepatic dysfunction (Kozic *et al.*, 2011).

The current study was aimed to compare liver function parameters in pregnant women with preeclampsia and normal pregnant women.

2 Materials and Methods

A hundred pregnant women ranging in age from 17 to 45 years were admitted to the Obstetrics and Gynaecology Department of the Medical Center at Al-Bayda in Northeast Libya. Cases were sampled from

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February 2019 to January 2020. The participants were split into two groups. Group A included 60 pre-eclampsia cases. After 20 weeks of gestation, Group B included 40 healthy pregnant women. Serum bilirubin levels as well as plasma levels of the liver enzymes ALT and AST were measured. A venous blood sample (5ml) was drawn at random from the pregnant women and placed in a sterile disposable syringe before being transferred to centrifuge tubes and allowed to clot for 30 minutes. The sample was centrifuged at 3000 rpm for 10 minutes to separate the serum, which was then stored at -20°C until analyzed. The serum was used to calculate alanine transaminase, aspartate transaminase, and bilirubin. The liver functions were determined using a Spectro-Photometer 4040V5+ chemical analyzer.

Statistical Analysis:

Minitab version 17 was used to analyze the data. The quantitative data were expressed as a mean ± SD, and percentage. The following statistics were performed: descriptive statistics and an independent samples t-test.

3 Results

Table (1) and Figures 1–4 show the liver function test parameters in the control and pre-eclampsia groups. The mean age in pre-eclampsia cases was 33.62, while it was 28.77 in controls. The mean AST value in pre-eclampsia cases was 22.53, while it was 15.63 in controls. The mean ALT level in pre-eclampsia patients was 24.08, while it was 16.00 in controls. The mean serum bilirubin level in pre-eclampsia patients was 0.550, while it was 0.533 in controls.

According to the current data, there was no significant difference in total bilirubin levels between the preeclampsia and control groups. However, at the end of the study, result found a significant difference in the ALT serum level between the preeclampsia and control groups ($p<0.05$), as well as a significant difference in the AST level between the two groups ($p<0.05$).

The mean value of headache symptoms in pre-eclampsia cases was 1.783, while it was 1.150 in controls. The mean value of visual symptoms in pre-eclampsia cases was 1.617, while it was 1.100 in controls. The mean value of chest pain in pre-eclampsia cases was 1.333, while it was 1.075 in controls. The mean value dyspnea in pre-eclampsia cases was 1.583, while it was 1.075 in controls. The mean value of nausea and vomiting in pre-eclampsia cases was 1.467, while it was 1.050 in controls. The mean value of epigastric pain in pre-eclampsia cases was 1.467, while it was 1.050 in controls. Table (2) depicts preeclampsia symptoms.

Among the 60 women diagnosed with preeclampsia, the number of women suffering from headache, vision disturbances, chest pain, dyspnea, nausea, vomiting and epigastric pain, respectively 47,37,20,35,28, and 28, and their percentages respectively 78.33, 61.67, 33.33, 58.33, 46.67, and 46.67, and the number of women who do not suffer from these symptoms, respectively 13,23,40,25,32, and 32, and their percentages, respectively 21.67, 38.33, 66.67, 41.67, 53.33, and 53.33. Table (3) demonstrates this.

The results of the correlation coefficient between the age of pre-eclamptic women and liver function parameters (LFT), and pre-eclampsia symptoms are presented in Table (4). Data found no link between the age of women with pre-eclampsia and their liver function disorder, as well as the symptoms associated with pre-eclampsia, implying that age plays no clear role in affecting the liver functions of women with pre-eclampsia and the symptoms associated with pre-eclampsia.

Result were used the box chart in this study because it is a convenient way of visually displaying the data distribution through their quartiles. The parallel lines extending from the boxes are known as "whiskers," and they are used to indicate variability outside the upper and lower quartiles. Outliers are sometimes plotted as individual dots that are in-line with whiskers.

Table (1). Comparison of liver function between control and pre-eclampsia groups

Parameter	Preeclampsia (60)	Control (n=40)	t-value	'p' - value
Age Mean ± SD	33.62 ± 6.50	28.77 ± 7.26	3.41	0.001*
AST (U/L) Mean ± SD	22.53 ± 9.97	15.63 ± 1.76	5.24	0.000*
ALT (U/L) Mean ± SD	24.08 ± 9.78	16.00 ± 4.28	5.64	0.000*
Serum Bilirubin (µmol/L) Mean ± SD	0.550 ± 0.362	0.533 ± 0.167	0.33	0.745

*Statistically significant: AST: Aspartate aminotransferase, ALT: Alanine aminotransferase.

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Table (2). Comparison of symptoms between control and pre-eclampsia groups.

Parameters	Preeclampsia (n=60)	Control (n=40)	t-value	'p' - value
Headache Mean± SD	1.783± 0.415	1.150± 0.362	8.08	0.000*
visual symptoms Mean ± SD	1.617± 0.490	1.100 ±0.304	6.50	0.000*
Chest pain Mean ± SD	1.333± 0.475	1.075± 0.267	3.47	0.001*
Dyspnea Mean ± SD	1.583± 0.497	1.075± 0.267	6.62	0.000*
Nausea and vomiting Mean ± SD	1.467± 0.503	1.050± 0.221	5.65	0.000*
Epigastric pain Mean ± SD	1.467± 0.503	1.050± 0.221	5.65	0.000*

*Statistically significant

Table (3). Comparison between women with preeclampsia who have symptoms of preeclampsia and women who do not have them.

Symptoms	Preeclamptic women with symptoms		Preeclamptic women without symptoms	
	Number	Percentage %	Number	Percentage %
Headache	47	78.33	13	21.67
Visual symptoms	37	61.67	23	38.33
Chest pain	20	33.33	40	66.67
Dyspnea	35	58.33	25	41.67
Nausea and vomiting	28	46.67	32	53.33
Epigastric pain	28	46.67	32	53.33

Table (4). The correlation between age and liver function parameters (LFT) and symptoms of pre-eclampsia.

LFT and symptoms	r	P value
AST/GOT for pre-eclampsia	-0.124	0.344
ALT/GPT for pre-eclampsia	-0.035	0.790
Total Bilirubin for pre-eclampsia.	0.084	0.524
Headache	0.113	0.391
Visual symptoms	-0.107	0.414
Chest pain	0.051	0.698
Dyspnea	-0.018	0.892
Nausea/vomiting	0.105	0.425
Epigastric pain	0.219	0.093

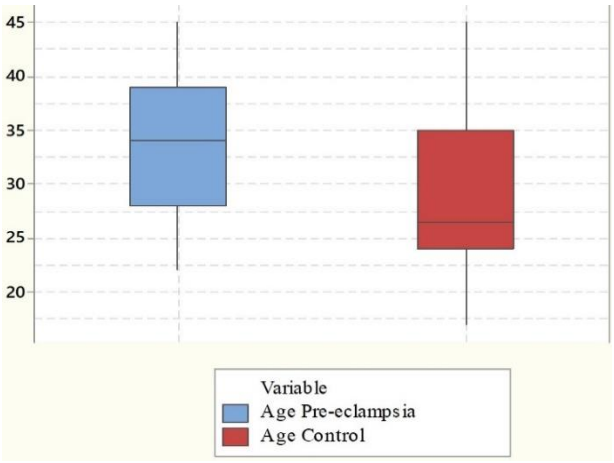

Figure (1). Boxplot for Age between pre-eclampsia and control groups

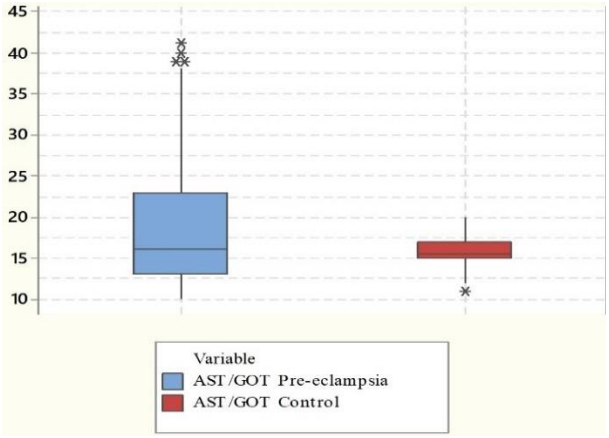

Figure (2). Boxplot for AST/GOT between pre-eclampsia and control groups.

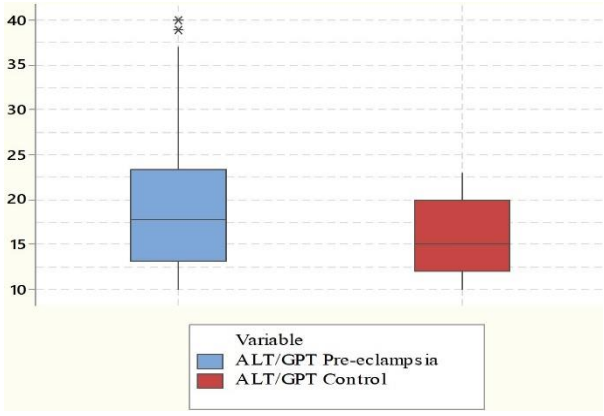

Figure (3). Boxplot for ALT/GPT between pre-eclampsia and control groups.

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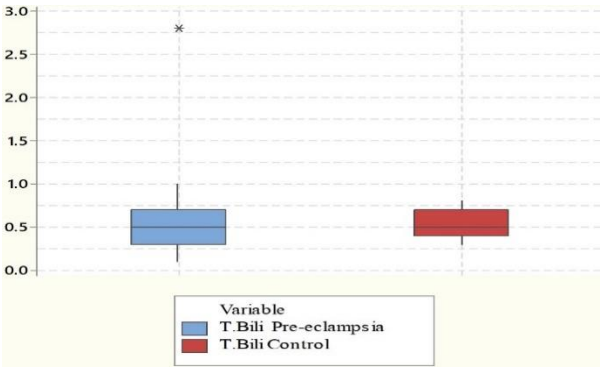

Figure (4). Boxplot for Total Bilirubin between pre-eclampsia and control groups.

4 Discussion

Although liver problems are uncommon in this disorder, severe preeclampsia is linked to perinatal illness and death. In fact, it is the most common cause of hepatic sensitivity and liver impairment during pregnancy, and 2%-12% of cases will develop HELLP syndrome, which manifests as the following three symptoms: hemolysis, elevated liver enzymes, and low platelet count.

Although liver involvement in preeclampsia does not necessitate treatment, it is an indicator to prevent more serious disorders such as eclampsia, hepatic rupture, or necrosis (Hay, 2008, and Hassanpour & Karami, 2018)**.** LFT are abnormal in 20% to 30% of pregnancies associated with preeclampsia (Borglin, 1958, Romero et al., 1989, and Hassanpour & Karami 2018) and are linked to poor maternal health and embryonic outcome. **(**Verhaeghe *et al*., 1991, Hay, 2008 and Hassanpour & Karami, 2018**).**

In the current study, LFT parameters such as ALT, AST, and total bilirubin in the two study groups were evaluated. The control group that consists of 40 healthy women with normal blood pressure and ages ranging between 17-45 years, in this group the levels of LFT parameters it was within normal limits, and the PE group, which included 60 women with PE, and their ages ranged between 22-45 years. (Patil *et al.* 2016).

In current study, observations wre found that there are statistically significant differences between the preeclampsia group and the control group in the level of ALT and AST enzyme, which was significantly elevated in the preeclampsia group when compared to the control group, and this is in line with the findings of Lodhi & Roy, 2018 in them study, where indicated that serum ALT and AST of pre-eclamptic women was significantly (P<0.001) elevated from their normotensive pregnant counterparts.

present results agrees with the results of (Malvino *et al*.,2005) who said that in pre-eclampsia the serum transaminase level was raised to >10 U/L and that of ALT to 271±297 U/L and Serum AST level in pre-eclampsia was also found more than 70 U/L which rose up to 209±178 U/L in eclampsia. Hassanpour & Karami (2018) showed that there was a significant difference in the serum ALT level between normotensive pregnant women and preeclampsia pregnant women (*p<0.05*). Ohotu *et al.* (2023) they recorded significant increase in the liver enzymes involving the ALT and AST and Alkaline Phosphatase (ALP) levels in the preeclamptic patients compared to the non-preeclamptic controls.

Khan *et al.* (2023) observed in their study that (ALT and AST) were significantly elevated among preeclamptic women (p<0.05). According to Munazza *et al*. (2011) and Patil *et al*. (2016), severe preeclamptic and eclamptic women had serum ALT levels that were significantly (*P<0.001*) higher than those of normotensive pregnant women, and preeclamptic cases had mean serum AST levels that were significantly (*P<0.001*) higher than the normotensive control group.

According to Dacaj *et al.* (2016), pregnant women with PE had statistically significant higher levels of AST, ALT, LDH, and total cholesterol than pregnant women in good health. When researching severe preeclampsia. Rath *et al*. (2000) found that the enzymes ALT and AST activities were both increased. In preeclamptic gestation, Makoyana *et al*. (2002) also noted elevation in AST and ALP activities.

Based on a study by Panda & Mondal, (2018), whose goal was to compare the results of liver and kidney function tests among preeclampsia patients between the ages of <35 and ≥35 years, in contrast to our finding, they found that the mean serum ALT levels in both the control and study groups were within the normal range. However, the mean AST and mean ALP levels revealed elevated values in both groups, which is consistent with our finding regarding AST. Makuyana *et al*. (2002) disagreed with current result at a compared liver function in normal and preeclamptic gestation, that did not notice differences in the level of ALT.

The influence of hypoxia on the liver during preeclamptic pregnancy accounts for the elevated serum level of AST in PE. Endothelium disruption causes prostacyclin levels to drop and thromboxane levels to rise. The ratio of PgI2/TxA2 is increased in favor of thromboxane, causing the liver's blood arteries to constrict. The consequences of hypoxia on the liver will result in hepatocyte necrosis and degeneration, which will raise AST levels. PE results in the release of several mediators (fibronectin, thrombomodulin, endothelin-l, and thromboxane) from the liver and blood vessel endothelium, which results in vasoconstriction and hepatic hypoxia, hypoxia raises the level of ALT

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According to (Cines *et al*.,1998, Dacaj *et al*., 2016, Patil *et al*., 2016 and Lodhi & Roy, 2018).

Shukla *et al*. (1978) and Hassanpour & Karami, (2018) mentioned that in normal gestation, ALT and AST are lower than in non-pregnant age-matched women, however, AST changes to a lesser amount. Mcmahon *et al*. (1993) and Hassanpour & Karami, (2018) pointed out that the primary fluctuations in liver function evaluation may be due to red cell demolition and ultimately happens liver damage. showed their results that liver damage in pregnant women with PE, and other biomarkers were higher in pregnant women with PE compared with normal pregnant women.

In this investigation, there were no statistically significant differences between the control group and the preeclampsia group in terms of T.B. levels. These findings are in line with those of Makuyana *et al*. (2002), who observed no differences in serum bilirubin when they evaluated liver function in normal and preeclamptic gestation. Patil *et al*. (2016) found that liver function parameters were significantly elevated in the severe preeclampsia and eclampsia group except for serum bilirubin level, which is not significantly higher when compared with the control group of the same age.

On other hand, present findings differ from those of Lodhi & Roy, (2018) who found that the concentration of serum bilirubin was considerably greater ($P<0.001$) in pre-eclampsia patients prior to delivery than in the control group of same-age and parity individuals with normal blood pressure, and also differs from the results of Malvino *et al.* (2005) who indicated that in HELLP syndrome serum bilirubin concentration was elevated from its normal value to about >1.2 mg/dl. Similar findings were made by Jaleel *et al.* (1999) and Munazza *et al*. (2011), showing pre-eclamptic women had significantly higher serum bilirubin levels than normotensive pregnant women. Hassanpour & Karami, (2018) also found that although direct bilirubin levels were not significantly different from the normal group, total bilirubin levels were higher in pregnant women with PE.

Various investigations have been examined the evaluation of liver function tests and liver damage in pregnant women with preeclampsia and normal pregnant women so that obtained different results. For example; a study by Girling *et al.* (1997) stated that the rate of liver function tests is less in normal gestation than the scope of reference presently used.

Girling *et al*, (1997) and Hassanpour & Karami, (2018) reported that AST, ALT, bilirubin, and GGT were each lower in uncomplicated pregnancy than in the non-pregnant laboratory reference ranges. In the pre-eclampsia group, 37% of the cases with higher liver function tests were abnormal only by the new reference ranges.

5 Conclusions

A frequent complication of pre-eclampsia is liver damage. While the amount of total bilirubin remained unaffected, we observed a disruption in some liver function indicators, where there was an increase in the activities of alanine transaminase and aspartate transaminase, which can be taken into account when predicting preeclampsia. To support the current theory, we propose additional research.

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Conflict of Interest: The authors declare that there are no conflicts of interest.

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