

Acute Fatty Liver of Pregnancy: A Life-Threatening Condition Requiring a Life-Saving Approach

Mansoureh Gorginzadeh,¹ Saeid Safari,² and Seyed Moayed Alavian^{3,4,*}

¹Department of Obstetrics and Gynecology, Tehran University of Medical Sciences, Tehran, IR Iran

²Department of Anesthesiology and Critical Care, Iran University of Medical Sciences, Tehran, IR Iran

³Baqiyatallah Research Center for Gastroenterology and Liver Diseases, Baqiyatallah University of Medical Sciences, Tehran, IR Iran

⁴Tehran Hepatitis Center, Tehran, IR Iran

*Corresponding author: Seyed Moayed Alavian, Baqiyatallah Research Center for Gastroenterology and Liver Diseases, Baqiyatallah University of Medical Sciences, Tehran, IR Iran. Tel: +98-2188945186, Fax: +98-2188945188, E-mail: alavian@thc.ir

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Dear Editor,

The accumulation of fatty acids in the hepatocytes, which is caused by different pathophysiologic mechanisms, is known as fatty liver disease. For instance, metabolic syndrome or obesity, in which lipolysis is suppressed as a result of hyperinsulinemia, would consequently provoke non-alcoholic fatty liver disease (NAFLD) or the more severe non-alcoholic steatohepatitis (NASH). In the long-term, this condition could result in liver cirrhosis (1, 2). However, when it occurs during the gestational period, it is termed acute fatty liver of pregnancy (AFLP). Rather than an indolent chronic disease, AFLP is a devastating condition that can rapidly progress to fulminant hepatic failure with associated coagulopathy or hepatic encephalopathy. In this scenario, the lives of two individuals (i.e., mother and infant) are inevitably jeopardized (3, 4).

With regards to AFLP, the underlying pathogenesis is unique. Maternal-fetal interactions are mostly blamed for the impaired fatty acid beta-oxidation. Indeed, fatty acid oxidation defects have been associated with maternal liver dysfunction (5-8). These defects are autosomal recessive. The most common such defect is an inherited deficiency of a mitochondrial enzyme, namely long-chain 3-hydroxyacetyl coenzyme-A dehydrogenase (LCHAD), which leads to the accumulation of toxic long-chain fatty acids in the woman's liver. Hepatocyte failure will ultimately ensue. The oxidative stress begins in the placenta (3, 8), although it can also affect the neonate (9).

Since its initial description in 1940, AFLP has been considered an obstetric emergency that can lead to multiple organ failure in a short time unless it is diagnosed promptly (3, 4). The diagnosis of AFLP is based on the Swansea criteria, which represent a constellation of signs and symptoms, along with abnormal lab tests such as el-

evated aminotransferases (10). As a disease of the last trimester of pregnancy, AFLP presents with intriguing features, including non-specific gastrointestinal symptoms that are easily overlooked or misdiagnosed (3, 7, 11). Therefore, defining appropriate screening guidelines for outpatient pregnant women could be life-saving. The 34th week of gestation has been recommended for this purpose (12). As the first step, liver and coagulation function tests could be performed for any pregnant woman who complains of new-onset gastrointestinal symptoms such as abdominal pain, nausea, and vomiting. If abnormal results are found, further tests should be performed, including renal function tests, blood glucose level, and abdominal ultrasound (5, 11-13).

Unlike HELLP syndrome and severe preeclampsia, which are the other potentially fatal disorders unique to the last trimester of pregnancy and puerperium, AFLP is a true hepatic dysfunction. Hence, impaired coagulation function tests should be more prominent as they could have prognostic value (5, 13, 14). In a study by Meng et al. involving 43 patients managed in a tertiary care center, the levels of prothrombin time, plasma fibrinogen, and platelet counts were correlated with the recovery time, while the leukocyte count, serum blood glucose, and hepatic aminotransferase levels showed no value in predicting the prognosis (14). Emergency termination of the pregnancy is the cornerstone of AFLP management, with cesarean section being the preferred mode of delivery. Nevertheless, the correction of concurrent coagulopathy with adequate blood products should be considered first (4, 7, 8). The transfusion of fresh frozen plasma (FFP), cryoprecipitate, or platelet concentrates in the case of abnormal conventional tests like prothrombin time (PT), activated partial thromboplastin time (aPTT), or fibrinogen could

prevent further bleeding complications. However, there remain some concerns regarding fluid overload, acute lung injury, and infection as a result of the use of these products (15). Moreover, the current standard coagulation tests are considered to be only weak predictors of bleeding in critically ill patients; therefore, additional methods such as thromboelastometry could be employed (16, 17). Thromboelastometry has been applied in the early prediction of bleeding complications in severely ill patients. In a case report by Crochemore et al., this method was found to efficiently detect the hypocoagulable state and diminished fibrinogen function quality at the beginning of surgery. Fibrinogen and prothrombin complex concentrates were administered to the patient and the cesarean section was performed without any major bleeding (17). The injection of recombinant factor 7 along with supportive care management in an intensive care unit has been also recommended (18). Through the application of plasma exchange and plasma perfusion during the early phase of AFLP, the progression of the disease can be stopped or reversed (19).

Another important point concerns the deficiency of vitamin K observed in neonates born to women with AFLP. There has been a case report of severe intracranial bleeding due to early vitamin K deficiency in a neonate whose mother was diagnosed with AFLP. In a study by Arya et al. (20), it was suggested that monitoring infants born to these women could be helpful in reducing their morbidity and mortality.

In sum, it is important to note that the management of AFLP is a multidisciplinary progress that necessitates active and prompt intervention by gastroenterologists and anesthesiologists along with obstetricians and neonatologists in a tertiary care center equipped with an intensive care unit (9, 13, 18). While as deleterious as both preeclampsia and HELLP syndrome, AFLP differs in that its management requires more than just the termination of the pregnancy. Hence, the monitoring of both the mother and her neonate for several days following delivery is vital. Furthermore, considering the fact that unlike more benign diseases such as NAFLD or NASH, the progression to cirrhosis in AFLP has not been reported until now (1, 3), the timely intervention of professionals should result in there being no long-term sequelae.

Footnote

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References

- Engelmann G, Hoffmann GF, Grulich-Henn J, Teufel U. Alanine aminotransferase elevation in obese infants and children: a marker of early

- onset non alcoholic Fatty liver disease. *Hepat Mon.* 2014;**14**(4):14112. doi: [10.5812/hepatmon.14112](https://doi.org/10.5812/hepatmon.14112). [PubMed: [24748893](https://pubmed.ncbi.nlm.nih.gov/24748893/)].
- Bugianesi E, McCullough AJ, Marchesini G. Insulin resistance: a metabolic pathway to chronic liver disease. *Hepatology.* 2005;**42**(5):987-1000. doi: [10.1002/hep.20920](https://doi.org/10.1002/hep.20920). [PubMed: [16250043](https://pubmed.ncbi.nlm.nih.gov/16250043/)].
- Xiong HF, Liu JY, Guo LM, Li XW. Acute fatty liver of pregnancy: over six months follow-up study of twenty-five patients. *World J Gastroenterol.* 2015;**21**(6):1927-31. doi: [10.3748/wjg.v21.i6.1927](https://doi.org/10.3748/wjg.v21.i6.1927). [PubMed: [25684961](https://pubmed.ncbi.nlm.nih.gov/25684961/)].
- Vigil-de Gracia P, Montufar-Rueda C. Acute fatty liver of pregnancy: diagnosis, treatment, and outcome based on 35 consecutive cases. *J Matern Fetal Neonatal Med.* 2011;**24**(9):1143-6. doi: [10.3109/14767058.2010.531325](https://doi.org/10.3109/14767058.2010.531325). [PubMed: [21668324](https://pubmed.ncbi.nlm.nih.gov/21668324/)].
- Riely CA. Liver disease in the pregnant patient.. *Am J Gastroenterol.* 1999;**94**(7):1728-32. doi: [10.1111/j.1572-0241.1999.01199.x](https://doi.org/10.1111/j.1572-0241.1999.01199.x). [PubMed: [10406228](https://pubmed.ncbi.nlm.nih.gov/10406228/)].
- Shah JM, Mehta MN, Viradiya HB. Acute fatty liver of pregnancy. *IJCP.* 2013;**23**(9):550-2.
- Kamimura K, Abe H, Kawai H, Kamimura H, Kobayashi Y, Nomoto M, et al. Advances in understanding and treating liver diseases during pregnancy: A review. *World J Gastroenterol.* 2015;**21**(17):5183-90. doi: [10.3748/wjg.v21.i17.5183](https://doi.org/10.3748/wjg.v21.i17.5183). [PubMed: [25954092](https://pubmed.ncbi.nlm.nih.gov/25954092/)].
- Goel A, Jamwal KD, Ramachandran A, Balasubramanian KA, Eapen CE. Pregnancy-related liver disorders. *J Clin Exp Hepatol.* 2014;**4**(2):151-62. doi: [10.1016/j.jceh.2013.03.220](https://doi.org/10.1016/j.jceh.2013.03.220). [PubMed: [25755551](https://pubmed.ncbi.nlm.nih.gov/25755551/)].
- Kobayashi T, Minami S, Mitani A, Tanizaki Y, Booka M, Okutani T, et al. Acute fatty liver of pregnancy associated with fetal mitochondrial trifunctional protein deficiency. *J Obstet Gynaecol Res.* 2015;**41**(5):799-802. doi: [10.1111/jog.12609](https://doi.org/10.1111/jog.12609). [PubMed: [25420603](https://pubmed.ncbi.nlm.nih.gov/25420603/)].
- Cowie P, Johnston IG. Acute Fatty Liver of Pregnancy. London: ATOTW; 2010. pp. 1-5.
- Ko H, Yoshida EM. Acute fatty liver of pregnancy. *Can J Gastroenterol.* 2006;**20**(1):25-30. [PubMed: [16432556](https://pubmed.ncbi.nlm.nih.gov/16432556/)].
- Zhu T, Li Q, Zhang W, Huang J, Peng Q, Liu Y, et al. Screening time and schedule for outpatients with acute fatty liver of pregnancy. *Zhong Nan Da Xue Xue Bao Yi Xue Ban.* 2015;**40**(7):748-53. [PubMed: [26267687](https://pubmed.ncbi.nlm.nih.gov/26267687/)].
- Mohammad Jafari R, Saadati N, Rezaie M. Acute Fatty Liver of Pregnancy: A Clinical-Paraclinical Survey. *IJHR.* 2015;**6**(1) doi: [10.5812/ijhr.27808](https://doi.org/10.5812/ijhr.27808).
- Meng J, Wang S, Gu Y, Lv H, Jiang J, Wang X. Prenatal predictors in postpartum recovery for acute fatty liver of pregnancy: experiences at a tertiary referral center. *Arch Gynecol Obstet.* 2016;**293**(6):1185-91. doi: [10.1007/s00404-015-3941-5](https://doi.org/10.1007/s00404-015-3941-5). [PubMed: [26525698](https://pubmed.ncbi.nlm.nih.gov/26525698/)].
- Association of Anaesthetists of Great Britain and Ireland, Thomas D, Wee M, Clyburn P, Walker I, et al. Blood transfusion and the anaesthetist: management of massive haemorrhage. *Anaesthesia.* 2010;**65**(11):1153-61. [PubMed: [20963925](https://pubmed.ncbi.nlm.nih.gov/20963925/)].
- Stainsby D, Jones H, Asher D, Atterbury C, Boncinelli A, Brant L, et al. Serious hazards of transfusion: a decade of hemovigilance in the UK. *Transfus Med Rev.* 2006;**20**(4):273-82. doi: [10.1016/j.tmr.2006.05.002](https://doi.org/10.1016/j.tmr.2006.05.002). [PubMed: [17008165](https://pubmed.ncbi.nlm.nih.gov/17008165/)].
- Crochemore T, de Toledo Piza FM, Silva E, Correa TD. Thromboelastometry-guided hemostatic therapy: an efficacious approach to manage bleeding risk in acute fatty liver of pregnancy: a case report. *J Med Case Rep.* 2015;**9**(1):202. doi: [10.1186/s13256-015-0690-9](https://doi.org/10.1186/s13256-015-0690-9). [PubMed: [26395443](https://pubmed.ncbi.nlm.nih.gov/26395443/)].
- K S, Thunga S, Narayanan A, Singh P. Recombinant activated factor VII in the management of acute fatty liver of pregnancy: A case report. *J Obstet Gynaecol Res.* 2015;**41**(7):1122-5. doi: [10.1111/jog.12684](https://doi.org/10.1111/jog.12684). [PubMed: [25809227](https://pubmed.ncbi.nlm.nih.gov/25809227/)].
- Ding J, Han LP, Lou XP, Geng LN, Liu D, Yang Q, et al. Effectiveness of combining plasma exchange with plasma perfusion in acute fatty liver of pregnancy: a retrospective analysis. *Gynecol Obstet Invest.* 2015;**79**(2):97-100. doi: [10.1159/000368752](https://doi.org/10.1159/000368752). [PubMed: [25634306](https://pubmed.ncbi.nlm.nih.gov/25634306/)].

20. Arya S, Richardson CJ, Jain S, Swischuck LE. Early Vitamin K Deficiency Bleeding in a Neonate Associated with Maternal Acute Fatty Liver

of Pregnancy. *AJP Rep.* 2015;5(2):193-5. doi: [10.1055/s-0035-1557107](https://doi.org/10.1055/s-0035-1557107). [PubMed: [26495183](https://pubmed.ncbi.nlm.nih.gov/26495183/)].

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